UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

CENTERWELL PHARMACY, INC., Plaintiff, v. CELGENE CORPORATION and BRISTOL MYERS SQUIBB COMPANY, Defendants.	Civil Action No. _____ JURY TRIAL DEMANDED

COMPLAINT

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Plaintiff CenterWell Pharmacy, Inc. ("CenterWell") hereby sues Celgene Corporation and Bristol Myers Squibb Company. CenterWell alleges, based on personal knowledge of facts known to it, and upon information and belief based on reasonable investigation, as follows:

I. INTRODUCTION

1. This civil action arises from pharmaceutical giants Bristol Myers Squibb Company's ("BMS") and Celgene Corporation's ("Celgene") overarching monopolistic scheme to unlawfully extend a monopoly in the market for pomalidomide, a blockbuster drug sold under the brand name Pomalyst that is used to treat the blood cancer multiple myeloma. Celgene and BMS accomplished the scheme through (i) a pattern of fraud on the U.S. patent office, (ii) abuse of the federal judicial system via sham litigations, and (iii) eventually settling with generic competitors for extended delay of generic entry for years through agreements that lock in unlawful supra-competitive pricing. As a result, CenterWell has overpaid and continues to overpay for a $2.25 billion-a-year-drug that should have faced vigorous generic competition years ago.

2. *Fraud on the U.S. patent office.* The fraud on the U.S. patent office involved Celgene fraudulently acquiring two series of pomalidomide patents, one for methods-of-using the drug and the other for formulations of it. Celgene misrepresented and concealed information that had already been in the public domain about the properties, formulations, and potential uses of pomalidomide from PTO examiners. Celgene and its agents knew their misrepresentations and concealment were false because they had been involved in the prior research themselves or because Celgene purchased rights to earlier, prior art research. Had the fraud not occurred, the patents would not have issued, and generic pomalidomide would have been available sooner than it will be.

3. *Abuse of the federal judicial system.* Celgene misused the federal judicial system by filing a series of sham lawsuits, using the pomalidomide method-of-use and formulation patents, along with inapplicable polymorph patents, against potential incumbent generic companies that sought to enter

the U.S. market for pomalidomide. The lawsuits were a sham because: (i) regardless of whether the patents had been procured by fraud, Celgene had no realistic likelihood of prevailing since full factual disclosure during federal litigation would have shown the patents to be invalid and/or non-infringed, and (ii) Celgene's purpose in bringing the lawsuits was not to prevail on the merits; rather it was to block the generic companies' attempt to gain market entry. Had the sham lawsuits not been filed and continued, generic manufacturers would not have been impeded, and generic pomalidomide would have been available sooner than it will be.

4. *Reverse payments to, and market allocation with, would-be competitors.* The anticompetitive reverse payment settlements happened in the wake of Celgene's sham litigations against its would-be generic competitors. After acquiring Celgene, BMS knew that Celgene would not prevail in the patent litigation, so Celgene and BMS paid off several of the first-to-file generic companies—including Aurobindo, Eugia, Breckenridge, Natco, and Teva—to terminate these companies' challenges to the bogus pomalidomide patents and ensure anticompetitive delay in market entry by would-be competitors. While the form of the payment in the deals were carefully cloaked by absolute secrecy, each of them amounted to unlawful market allocation agreements by allocating the pomalidomide market through carefully timed limited entry by the generic companies. Had Celgene and BMS not paid off their would-be competitors, generic pomalidomide would have been available sooner than it will be.

5. Taken individually or together, the alleged conduct violated, and continues to violate, the federal Sherman Act and State trade practices acts and common law. CenterWell seeks monetary relief in the form of damages and restitution. And because the effect of the wrongdoing is ongoing, CenterWell also seeks injunctive relief.

II. PARTIES

6. Plaintiff CenterWell Pharmacy, Inc., f/k/a Humana Pharmacy, Inc., f/k/a Rightsource ("CenterWell") is incorporated in the state of Delaware and is headquartered at 500 West Main Street, Louisville, Kentucky. CenterWell buys prescription drugs directly from manufacturers and wholesalers and dispenses them through its specialty pharmacy to parent company Humana Inc.'s and other payers' plan members. Through the ordinary course of its pharmacy business, CenterWell has purchased and then dispensed Pomalyst directly from Defendants Celgene and BMS pursuant to contractual agreements.

7. Defendant Bristol Myers Squibb Company ("BMS") is a pharmaceutical company organized and existing under the laws of the State of Delaware. During most times relevant to the Complaint, BMS maintained its principal executive offices at 430 E. 29th Street, 14FL, New York, NY 10016. BMS has since changed its principal executive offices to Route 206 & Province Line Road, Lawrenceville, New Jersey 08543.

8. Defendant Celgene Corporation is a pharmaceutical company organized and existing under the laws of the State of Delaware with a principal place of business at 86 Morris Avenue, Summit, New Jersey 07901. In 2019, Celgene Corporation was acquired by, and became a wholly owned subsidiary of, BMS. Celgene Corporation, whether before or after its acquisition by BMS, is referred to as "Celgene."

III. JURISDICTION AND VENUE

9. This Court has jurisdiction over this action pursuant to 15 U.S.C. §§ 15 and 26, and 28 U.S.C. §§ 1331 and 1337. CenterWell asserts federal claims for treble damages, injunctive relief, and costs of suit, including reasonable attorneys' fees, against Defendants under Section 2 of the Sherman Act, 15 U.S.C. § 2, and Sections 4 and 16 of the Clayton Act, 15 U.S.C. §§ 15 and 26.

10. This Court has personal jurisdiction over Defendants because Defendants are present in the United States, do business in the United States, have registered agents in the United States, may be found in the United States, and are otherwise subject to the service of process provisions of 15 U.S.C. § 22. Each Defendant has transacted business, maintained substantial contacts, and/or committed overt acts in furtherance of the illegal scheme and conspiracy throughout the United States, including in this district. The scheme and conspiracy have been directed at, and have had the intended effect of, causing injury to persons residing in, located in, or doing business throughout the United States, including in this district.

11. Venue is appropriate within this district under Section 12 of the Clayton Act, 15 U.S.C. §§ 15(a) and 22, and 28 U.S.C. § 1391. During the relevant period, Defendants resided, transacted business, or had agents in this district.

IV. REGULATORY FRAMEWORK

A. The regulatory structure for approval of generic drugs balances the benefits of inducing new drug innovation and generic drug competition.

12. Under the federal Food, Drug, and Cosmetic Act (FDCA),[1] manufacturers that create a new drug must secure approval from the Food and Drug Administration (FDA) to sell the product by filing a New Drug Application (NDA).[2] An NDA must include detailed data concerning the safety and effectiveness of the drug, as well as any information on applicable patents.[3]

13. When the FDA approves a brand manufacturer's NDA, the manufacturer may list certain kinds of patents that the manufacturer asserts could reasonably be enforced against a generic manufacturer that makes, uses, or sells a generic version of the brand drug before the expiration of

[1] Pub. L. No. 75-717, 52 Stat. 1040 (1938) (codified as amended in 21 U.S.C. § 301 *et seq.*).

[2] 21 U.S.C. §§ 301-392.

[3] 21 U.S.C. § 355(a), (b).

the listed patents in *Approved Drug Products with Therapeutic Equivalence Evaluations* (known as the "Orange Book").[4] The manufacturer may also list additional patents in the Orange Book after the FDA has approved an NDA within 30 days of issuance of such patents..[5] While valid and infringed patents may lawfully prevent generic competition, at least for a period, manufacturers may not abuse the system by using invalid or non-infringed patents to unlawfully delay generic competition. Doing so upsets the balance struck by Congress in the Drug Price Competition and Patent Term Restoration ("Hatch-Waxman") Act between incentivizing research and development of new therapies and encouraging competition among pharmaceutical companies.

14. The FDA relies entirely on the brand manufacturer's truthfulness about patent validity and applicability because it does not have the resources, authority, or expertise to verify the manufacturer's patents for accuracy or trustworthiness. In listing patents in the Orange Book, the FDA performs a purely ministerial act.

1. Congress designed the Hatch-Waxman Amendments to the FDCA to hasten generic entry and reduce healthcare costs.

15. The FDCA's Hatch-Waxman Amendments, enacted in 1984, simplified regulatory hurdles for prospective generic manufacturers by eliminating the need to file lengthy and costly NDAs.[6] A manufacturer seeking approval to sell a generic version of a brand drug instead files an Abbreviated New Drug Application (ANDA). An ANDA relies on the scientific findings of safety and effectiveness included in the brand sponsor's NDA and must merely show that the proposed generic formulation contains the same active ingredient(s), dosage form, route of administration, and

[4] For example, patents covering processes for making drug products do not qualify for listing in the Orange Book.

[5] 21 U.S.C. §§ 355(b)(1), (c)(2).

[6] *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified, as amended, at 21 U.S.C. § 355).

strength as the reference branded drug and that it is bioequivalent, *i.e.*, absorbed at the same rate and to the same extent as the brand.

16. Drug products that the FDA considers therapeutically equivalent to the reference drug product are assigned an "A" code. This assignment includes products for which "there are no known or suspected bioequivalence problems" (AA, AN, AO, AP, or AT, depending on how the drug is administered) and drug products for which "actual or potential bioequivalence problems have been resolved with adequate *in vivo* and/or *in vitro* evidence supporting bioequivalence" (AB).[7]

17. The FDCA and Hatch-Waxman Amendments operate on the principle that bioequivalent drug products containing identical amounts of the same active ingredients, having the same route of administration and dosage form, and meeting applicable standards of strength, quality, purity, and identity are therapeutically equivalent and may be substituted for one another without the approval of a prescribing physician.

18. Through the Hatch-Waxman Amendments, Congress sought to expedite the entry of less expensive generic competitors to brand drugs, thereby reducing healthcare expenses nationwide. Congress also sought to protect pharmaceutical manufacturers' incentives to create new and innovative products.

19. The Hatch-Waxman Amendments achieved both goals, substantially elevating the rate of generic product launches while simultaneously ushering in an era of historically high profit margins for brand pharmaceutical manufacturers. In 1983, before the Hatch-Waxman Amendments, only 35% of the top-selling drugs with expired patents had generic alternatives; by 1998, nearly all did. In 1984, revenues for brand and generic prescription drugs totaled $21.6 billion; by 2013, total prescription drug revenues had climbed to more than $329.2 billion, with generics accounting for

[7] FDA, *Orange Book Preface*, available at https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface (last accessed August 21, 2024).

86% of prescriptions.[8] Generics are dispensed about 95% of the time when a generic form is available.[9]

2. The FDA may grant regulatory exclusivities for new drugs, but those exclusivities do not necessarily bar generic entry.

20. To promote a balance between new drug innovation and generic drug competition, the Hatch-Waxman Amendments also provide for exclusivities (or exclusive marketing rights) for new drugs. The FDA grants these exclusivities upon approval of a drug if the sponsor and/or drug meet the relevant statutory requirements. Any such exclusivities for a drug are listed in the Orange Book, along with any applicable patents, and can run concurrently with the listed patents.

21. One such exclusivity, the New Chemical Entity (NCE) exclusivity, applies to products containing chemical entities never previously approved by the FDA either alone or in combination with another chemical entity. If a product receives NCE exclusivity, the FDA may not accept for review any ANDA for a drug containing the same active moiety for five years from the date of the NDA's approval.[10] If the patent holder filed a patent infringement suit filed within the one-year period beginning four years after NDA approval, the 30-month stay is extended by amount of time such that a total of 7.5 years will elapse from the date of NDA approval.

22. A drug product may also receive a three-year period of exclusivity if its sponsor submits a supplemental application (sNDA) that contains reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to approval of the supplemental application. If this exclusivity is granted, the FDA may not approve an

[8] *See* IMS Institute for Healthcare Informatics, *Medicine Use and Shifting Costs of Healthcare: A Review of the Use of Medicines in the United States in 2013* 30, 51 (2014).

[9] *Id.* at 51.

[10] Unless the ANDA contains a certification of patent invalidity or non-infringement in which case an application may be submitted after four years. 21 U.S.C. § 355(j)(5)(F)(ii); 21 C.F.R. § 314.108(b)(2).

ANDA for that drug for three years from the date on which the supplemental application is approved.[11]

23. Regulatory exclusivities may not be absolute bars to generic entry. For example, some can be overcome by carving out information in the label or for other reasons.[12]

3. Abbreviated New Drug Applications must be accompanied by a certification under paragraphs I, II, III, and/or IV, the last of which can trigger an automatic stay of FDA approval.

24. To obtain FDA approval of an ANDA, a manufacturer must certify that the generic will not infringe any patents listed in the Orange Book. Under the Hatch-Waxman Amendments, a generic manufacturer's ANDA must contain one of four certifications:

a. That no patent for the brand has been filed with the FDA (a paragraph I certification);

b. That any patent(s) for the brand has/have expired (a paragraph II certification);

c. That any patent(s) for the brand will expire on a particular date and the manufacturer does not seek to market its generic before that date (a paragraph III certification); or

d. That any patent(s) for the brand is/are invalid or will not be infringed by the generic manufacturer's proposed product (a paragraph IV certification).[13]

25. If a generic manufacturer files a paragraph IV certification, a brand manufacturer can delay FDA approval of the ANDA just by suing the ANDA applicant for patent infringement. If the brand manufacturer initiates a patent infringement action against the generic filer within forty-five days of receiving notification of the paragraph IV certification, the FDA will not grant final approval to the ANDA-filer until the earlier of (i) the passage of two-and-a-half years, or (ii) the issuance of a decision by a court that the patent at issue is invalid or not infringed by the generic manufacturer's

[11] 21 U.S.C. § 355(j)(5)(F)(iv); 21 C.F.R. § 314.108(b)(2)(5).

[12] *See, e.g.*, 21 C.F.R. §§ 314.94(a)(8)(iv), 314.127(a)(7); 21 U.S.C. § 355a(o).

[13] 21 U.S.C. § 355(j)(2)(A)(vii).

ANDA.[14] Until one of those conditions occurs, the FDA may only grant tentative approval, meaning that the ANDA meets all regulatory requirements and is approvable but for the 30-month stay. FDA final approval may be delayed beyond the 30-month stay if the brand drug was entitled to the NCE exclusivity period.

26. Once the thirty-month stay ends (and the NCE exclusivity expires, if applicable) the FDA may grant an ANDA that meets all regulatory requirements final approval. Once the ANDA has received final approval, the generic manufacturer may launch its product, even if the patent litigation is still pending. This is known as an "at-risk" generic launch, the "risk" being that the generic manufacturer will have to pay the brand manufacturer its lost profits if the generic manufacturer launches its generic and later loses the patent litigation. However, where the generic manufacturer expects to ultimately prevail in the patent litigation, it is highly incentivized to launch at-risk. In one study of the 42 generic drugs that had received FDA approval and were not prevented by an injunction from launching, nearly two-thirds launched at risk.[15]

4. The first ANDA filer to issue a paragraph IV certification, once approved, is entitled to 180 days as the only ANDA generic on the market.

27. To encourage manufacturers to seek approval of generic versions of brand drugs, the Hatch-Waxman Amendments grant the first paragraph IV generic manufacturer ANDA filer (first-filer) a 180-day exclusivity period to market its generic version of the drug. During that time, the

[14] 21 U.S.C. § 355(j)(5)(B)(iii). This period is commonly called a 30-month Hatch-Waxman stay or 30-month stay. The brand/patent holder can choose to sue the generic after 45 days, including waiting until the generic has launched its product, but, in that event, the brand cannot take advantage of the 30-month stay of FDA approval, and must instead satisfy the showing required to obtain a preliminary injunction to prevent the generic launch.

[15] Keith M. Drake, Robert He, Thomas McGuire & Alice K. Ndikumana, *No Free Launch: At-Risk Entry By Generic Drug Firms,* National Bureau of Economic Research, Working Paper 29131, p. 18 (August 2021) ("Of the 42 generic drugs that had received FDA approval before a district court decision and were not prevented from entering by an injunction, 26 were launched at risk before a district court decision and 16 were not.") available at https://www.nber.org/papers/w29131.

FDA may not grant final approval to any other generic manufacturer's ANDA for the same brand drug.[16] That is, when a first-filer files a substantially complete ANDA certifying that the unexpired Orange Book patents covering the brand are invalid or not infringed, the FDA cannot approve a later generic manufacturer's ANDA until the first-filer has been on the market for 180 days. The first-filer's exclusivity period does not begin running until it, or another first filer, begins marketing its ANDA product.

28. A first-filer who informs the FDA it intends to wait until all Orange Book-listed patents expire before marketing its generic, does not get a 180-day exclusivity period. Congress created this 180-day period to incentivize generic manufacturers to challenge weak or invalid patents or to invent around such patents by creating non-infringing generics.

29. While the 180-day window is often referred to as the first-filer's six-month or 180-day exclusivity; that is a bit of a misnomer. A brand manufacturer can launch an authorized generic (AG) at any time, manufacturing its AG in accordance with its approved NDA for the branded product but selling at a lower price point. Also, the 180-day exclusivity period can be lost. One way a first-filer may forfeit its 180-day exclusivity is by failing to obtain tentative approval from the FDA for its ANDA within 30 months of the ANDA filing. But failure to obtain tentative approval within the specified time period does not always result in forfeiture. For example, if a change in the requirements for approval occurs, then the FDA may determine that the first-filer has not forfeited its exclusivity. The FDA will commonly defer a decision on forfeiture until it becomes necessary to decide the issue, typically when a later filer seeks final approval for its ANDA product. At that time, FDA must decide whether the first-filer has forfeited (clearing the way for final approval of the subsequent filer's ANDA) or whether the first-filer has not forfeited (in which case final approval

[16] 21 U.S.C. § 355(j)(5)(B)(iv), (D).

for the subsequent ANDA filer will be postponed until expiration of the first filer's 180-day exclusivity period).

5. Patents are intended to be subject to judicial and administrative scrutiny.

30. The existence of one or more patents purporting to cover a drug product does not guarantee a monopoly. Patents are routinely invalidated or held unenforceable, either upon reexamination, through *inter partes* proceedings by the U.S. Patent and Trademark Office (PTO), by court decision, or by jury verdict. A patent holder always bears the burden of proving infringement.

31. One way that a generic can prevail in patent infringement litigation is to show that its product does not infringe the patent (and/or that the patent holder cannot meet its burden to prove infringement). Another is to show that the patent is invalid or unenforceable.

32. A patent is invalid or unenforceable when: (i) the disclosed invention is anticipated and/or obvious in light of prior art; (ii) its claims are indefinite, lack sufficient written description, or fail to properly enable the claimed invention; (iii) an inventor, an inventor's attorney, or another person involved with the application, with intent to mislead or deceive the PTO, fails to disclose material information known to that person to be material, or submits materially false information to the PTO during prosecution; and/or (iv) when a later-acquired patent is not patentably distinct from the invention claimed in an earlier patent (and no exception, such as the safe harbor, applies) (referred to as "double patenting").

33. An assessment of whether a patent is obvious (and thereby invalid) depends on the prior art that existed as of the priority date of the claimed invention. "Prior art" refers to patents, published patent applications, and other non-patent sources, such as journal articles, that are publicly available. The "priority date" may be the date of the application for the claimed invention, or it may be an earlier date if the current patent application is a continuation of an earlier one.

34. If the PTO rejects a patent application as obvious, a patent applicant may seek to overcome that rejection by submitting evidence that the claimed invention shows unexpected results, that is, that the claimed invention is at odds with what one would expect based on existing science.

35. The patent examination process is *ex parte*, meaning that the patent examiner engages in a dialogue solely with the applicant. The public, third parties, and even researchers in the same field do not participate in the patent examination process. The patent process is therefore not an adversarial proceeding, and it resultingly lacks the safeguards of adverse parties presenting contrary evidence to the examiner.

36. Because the proceedings are *ex parte*, it is critical that the PTO receives all information from the applicant. To encourage a review of all relevant facts, the PTO imposes a strict duty of candor and good faith in all of the applicant's dealings with the PTO. As stated in the Manual of Patent Examining Procedure, "Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section."[17] Deceiving the PTO, engaging in inequitable conduct, including misleading the examiner, giving inaccurate statements during the prosecution, or violating the duty of disclosure, renders the patent invalid.

37. For all documents submitted to the PTO, the applicant, "whether a practitioner or non-practitioner," must certify that all statements from "the party's own knowledge" or "on information and belief" are true.[18] Additionally, the applicant must acknowledge that any statements made that "knowingly and willfully falsifies, conceals, or covers up by any trick, scheme, or device a

[17] 37 C.F.R. § 1.56(A) (2012).

[18] 37 C.F.R. § 11.18(a)-(b) (2021).

material fact, or knowingly and willfully makes any false, fictitious, or fraudulent statements or representations" will subject the applicant to penalties, including criminal penalties and "jeopardiz[ing] the probative value" of the filing.[19]

38. The PTO's decision to issue a patent does not substitute for a fact-specific assessment of (i) whether the applicant made intentional misrepresentations or omissions on which the PTO relied, and (ii) whether a reasonable manufacturer in the patent holder's position would have a realistic likelihood of succeeding on the merits of a patent infringement suit.

39. As a statistical matter, if the parties litigate a pharmaceutical patent infringement suit to a decision on the merits, it is much more likely that a challenged patent will be found invalid or not infringed than upheld. The FTC reports that generics prevailed in 73% of Hatch-Waxman patent litigation cases resolved on the merits between 1992 and 2002.[20] An empirical study of all substantive decisions rendered in every patent case filed in 2008 and 2009 similarly reports that when a generic challenger stays the course until a decision on the merits, the generic wins 74% of the time.[21]

40. If a generic manufacturer successfully defends against the brand's infringement lawsuit—either by showing that its ANDA does not infringe any asserted patents and/or that any asserted patents are invalid or unenforceable—the generic may enter the market immediately upon receiving approval from the FDA.

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[19] 37 C.F.R. § 11.18(b) (2021).

[20] FTC, *Generic Drug Entry Prior to Patent Expiration: An FTC Study* vi-vii (2002), available at https://www.ftc.gov/sites/default/files/documents/reports/generic-drug-entry-prior-patent-expiration-ftc-study/genericdrugstudy_0.pdf (last accessed August 21, 2024).

[21] John R. Allison, Mark A. Lemley & David L. Schwartz, *Understanding the Realities of Modern Patent Litigation*, 92 TEX. L. REV. 1769, 1787 (2014) ("[P]atentees won only 164 of the 636 definitive merits rulings, or 26%," and "that number is essentially unchanged" from a decade ago).

41. There is a predictable pattern to the way brand drug companies develop their patent portfolios for significant drugs. The first group of patents in the brand drug company's portfolio for the drug may reflect a genuine technological breakthrough that may later contribute to the success of the drug; these initial patents usually cover the active compound in a prescription drug or a particular pharmaceutical composition and may be correspondingly scientifically novel.

42. After filing applications for the original patents, the company continues its research and development efforts in the hopes of developing a drug product that could, eventually, be approved by the FDA. As the company's research matures, the patent filings continue, often for narrow modifications relating to specific formulations, methods of using the drug, or processes for creating the drug product disclosed in the original patent filings. But the original patent filings are now "prior art" and thus constrain the scope of valid follow-on patents. New patents can be obtained for features of the drug only if the brand drug company can show that the new features are non-obvious distinctions over the growing body of prior art, which includes patents and printed publications, among other things. Methods of using earlier inventions are seldom not disclosed by earlier compound or composition patents. Over time, as the number of patent filings for the drug grows, so too does the volume of prior art beyond which the brand drug company must show non-obvious distinctions.

43. Patents present obstacles for would-be generic competitors to design around. Some patents broadly cover a drug's active ingredient and – if valid and enforceable – may prove impossible to design around while meeting the FDA's criteria for equivalent generics. While generic versions of the brand product may be able to obtain FDA approval and enter the market before all patents expire, once all the valid patents covering its drug have expired, the brand drug company has no lawful means of preventing competitors from entering the market.

44. Therefore, a typical patent portfolio for a brand drug has its most significant patents issuing first; over time, the later-issued patents generally become increasingly narrow and more vulnerable to attack as invalid for covering subject matter that is old or obvious. Second- and third-generation patents with narrower coverage are more easily designed around by would-be generics, thus preventing the brand from satisfying its burden of proving patent infringement to keep generics out of the market.

B. AB-rated generics quickly and dramatically decrease prices for purchasers.

45. Generic versions of brand drugs contain the same active ingredient(s) as the brand name drug and are determined by the FDA to be just as safe and effective as their brand counterparts. Because the brand and its A-rated generics are essentially commodities that cannot be therapeutically differentiated, the primary basis for competition between a brand product and its generic version, or between multiple generic versions, is price.

46. Without A-rated generics in the market, the manufacturer of a brand drug has a monopoly—every sale of the product, and the accompanying profit, benefits the brand manufacturer. Without A-rated generic competition, brand manufacturers can, and routinely do, sell their drug for far more than the marginal cost of production, generating profit margins above 70% while making hundreds of millions of dollars in sales. The ability to command these kinds of profit margins is what economists call market power.

47. When generic entry occurs, the brand manufacturer loses most of the unit sales; the generic manufacturer sells most of the units, but at reduced prices (which continue to decline). When multiple generics compete in the market, that competition drives prices down to near the marginal cost of production. This competition ends the brand manufacturer's market power and delivers enormous savings to drug purchasers. Competition converts what formerly were excess profits into purchaser savings.

48. According to a recent FDA study,[22] "[f]irst-generics often yield substantial cost savings. Generic drugs approved in 2018 yield annual savings of $17.8 billion, with $4.0 billion from first-generic approvals. Savings from 2019 approvals amount to $24.8 billion, with $9.4 billion coming from first-generic approvals. Savings from 2020 approvals are estimated at $10.7 billion, with first-generic approvals contributing $1.8 billion. Over all three years, first-generic approvals account for 29% of the total savings." The FDA also highlighted the price reductions associated with generic drug approvals, reporting that it "observe[d] many instances where, within a year of the first-generic approval, prices fall by more than 75% compared to the brand price."

1. The first AB-rated generic is priced below the brand, driving sales to the generic.

49. Experience and economic research show that the first generic manufacturer to market its product prices it below the prices of its brand counterpart.[23] Every state requires or permits that a prescription written for the brand be filled with an A-rated generic. Thus, the first generic manufacturer almost always captures a large share of sales from the brand. At the same time, there is a reduction in the average price paid for the drug at issue (brand and A-rated generic combined).

50. During the 180-day exclusivity period, the first filer is the only ANDA-approved generic manufacturer on the market. In the absence of competition from other generics, a first-filer generic manufacturer generally makes about 80% of all the profits that it will ever make on the

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[22] Ryan Conrad PhD, et al., *Estimated Cost Savings from New Generic Drug Approvals in 2018, 2019, and 2020* (August 2022), available at https://www.fda.gov/media/161540/download#:~:text=Estimates%20of%20the%20total%2012,estimated%20%2410.7%20billion%20in%20savings (last accessed August 21, 2024).

[23] FTC, *Authorized Generic Drugs: Short-Term Effects and Long-Term Impact* ii-iii, vi, 34 (2011), available at https://www.ftc.gov/sites/default/files/documents/reports/authorized-generic-drugs-short-term-effects-and-long-term-impact-report-federal-trade-commission/authorized-generic-drugs-short-term-effects-and-long-term-impact-report-federal-trade-commission.pdf ("FTC 2011 AG Study") (last accessed August 21, 2024); FTC Pay-for-Delay Study at 1.

product during that 180-day exclusivity period, a significant incentive for getting to market as quickly as possible.

51. Once generic competition begins, it quickly captures sales of the corresponding brand drug, often 80% or more of the market within the first six months after entry. This percentage erosion of brand sales holds regardless of the number of generic entrants.

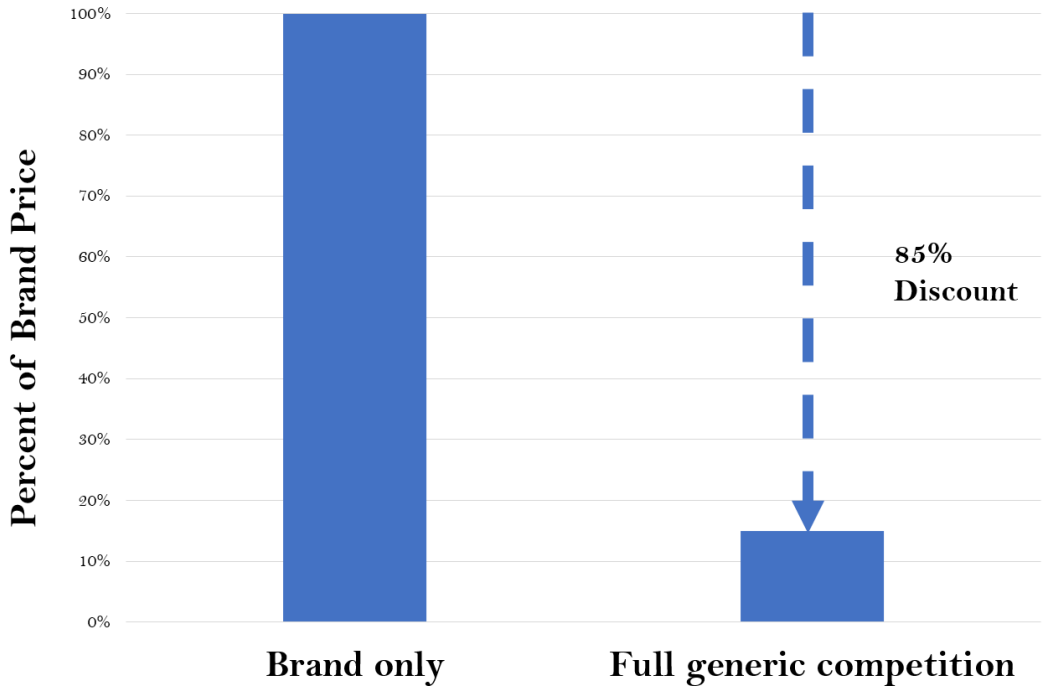
2. Later generics drive prices down further.

52. Once additional generic competitors enter the market, the competitive process accelerates, and multiple generic manufacturers typically compete vigorously with each other over price, driving prices down toward marginal manufacturing costs.[24] In a recent study, the Federal Trade Commission (FTC) found that on average, within a year of generic entry, generics had captured 90% of corresponding brand sales[25] and (with multiple generics on the market) prices had dropped 85%.[26]

[24] *See, e.g.*, Tracy Regan, *Generic Entry, Price Competition, and Market Segmentation in the Prescription Drug Market*, 26 INT'L J. INDUS. ORG. 930 (2008); Richard G. Frank, The Ongoing Regulation of Generic Drugs, 357 NEW ENG. J. MED. 1993 (2007); Patricia M. Danzon & Li-Wei Chao, *Does Regulation Drive Out Competition in Pharmaceutical Markets?*, 43 J.L. & ECON. 311 (2000).

[25] For blockbuster drugs, such as Pomalyst, generic market share after one year is often higher than 90%.

[26] *See* FTC Pay-for-Delay Study.



53. According to the FDA and the FTC, the greatest price reductions occur when the number of generic competitors goes from one to two. The price of the drug drops between 50% to 90% from the brand price when there are multiple generic competitors on the market for a given brand. Consequently, the launch of a generic usually results in significant cost savings for all drug purchasers: although generic drugs are chemically identical to their branded counterparts, they are typically sold at substantial discounts from the branded price.[27] According to the Congressional Budget Office, "generic drugs save consumers an estimated $8 to $10 billion a year at retail pharmacies. Even more billions are saved when hospitals use generics."[28]

[27] *See e.g.*, Conrad, R., and R. Lutter. (2019). *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices*. FDA, available at https://www.fda.gov/media/133509/download (last accessed August 21, 2024); Gupta, R., N. D. Shah and J. S. Ross. (2019). Generic Drugs in the United States: Policies to Address Pricing and Competition. *Clinical Pharmacology & Therapeutics*, 105 (2): 329-37.

[28] *See* "FDA Ensures Equivalence of Generic Drugs," FDA (August 2002), available at https://www.fda.gov/drugs/resources-drugs/fda-ensures-equivalence-generic-drugs.

54. Generic competition allows buyers of a drug to (i) purchase generic versions of the drug at substantially lower prices, and/or (ii) purchase the brand at a reduced price. These competitive effects are known and reliable: brand sales decline to a small fraction of their level before generic entry and, as a result, brand manufacturers view competition from generics as a grave threat to their bottom lines.

55. Until a generic version of a brand drug enters the market, however, there is no FDA-approved bioequivalent drug to substitute for and compete with the brand, leaving the brand manufacturer to continue to profit by charging supra-competitive prices. Recognizing that generic competition will rapidly erode their brand sales, brand manufacturers seek to extend their monopoly for as long as possible, sometimes resorting to illegal means to delay or prevent generic competition.

3. Authorized generics, like other generics, compete on price.

56. An "authorized generic" (AG) is a product sold under the authority of the brand's approved NDA. An AG is chemically identical to the brand drug but is sold as a generic, typically through either the brand manufacturer's subsidiary (if it has one) or through a third-party distributor.

57. If the 180-day exclusivity period applies to a first filer ANDA, the exclusivity exists only to bar the FDA from approving another ANDA during that time period. The exclusivity does not apply to products sold under the authority of the original NDA. As a result, the 180-day exclusivity does not bar the entry of authorized generics; the statutory scheme does not prevent a brand manufacturer from marketing and selling an AG at any time.

58. Brand manufacturers recognize the significant economic advantages of releasing their AGs to compete with the first-filer generic during the 180-day exclusivity period. One study

noted that "pharmaceutical developers facing competition from generics have large incentives to compete with their own or licensed 'authorized generics.'"[29]

59. Competition from an AG substantially reduces drug prices and the revenues of the first-filer generic (especially during the 180-day exclusivity period).

60. A study analyzing three examples of AGs found that "[f]or all three products, authorized generics competed aggressively against independent generics on price, and both the authorized and independent generics captured substantial market share from the brand."[30] The FTC similarly found that AGs capture a significant portion of sales, reducing the first-filer generic's revenues by about 50% on average. The first-filer generic makes much less money when it faces competition from an AG because (i) the AG takes a large share of unit sales away from the first filer; and (ii) the presence of the AG causes prices, particularly generic prices, to decrease.

61. Authorized generics are therefore a significant source of price competition. In fact, they are the only potential source of generic price competition during the first-to-file generic

[29] Kevin A. Hassett & Robert Shapiro, *The Impact of Authorized Generics on the Introduction of Other Generic Pharmaceuticals*, Sonecon LLC, 3 (May 2007) https://www.sonecon.com/wp-content/uploads/2022/01/050207_authorizedgenerics.pdf (last accessed August 21, 2024).

[30] Ernst R. Berndt, Richard Mortimer, Ashoke Bhattacharjya, Andrew Parece & Edward Tuttle, *Authorized Generic Drugs, Price Competition, and Consumer's Welfare*, 26 Health Affairs 790, 796 (2007).

manufacturer's 180-day exclusivity period. All drug industry participants recognize this. PhRMA recognizes it.[31] Generic companies recognize it.[32] Brand companies recognize it.[33]

V. FACTS

A. Development of thalidomide and its analogs, including pomalidomide, for the treatment of cancers.

62. The following eleven sections of the Complaint (sub-headings 1 through 11) allege facts regarding the state of known science regarding pomalidomide, its uses and its formulation, through November 2002 when Celgene filed the first in a series of fraudulent patent applications to cover uses and formulations of pomalidomide. Indeed, by November 2002, pomalidomide had already been disclosed, its use for various purposes (including multiple myeloma) reported, and its known but modest product formulation challenges well known. Yet, Celgene, along with Anthony Insogna (a principal attorney in the fraudulent patent prosecutions) and Jerome Zeldis (Celgene's medical director and the ostensible inventor for some of the fraudulently acquired patents) had personal and significant knowledge regarding these public disclosures and prior art, and knew that

[31] Brand industry lobbying group PhRMA sponsored a study that concludes that the presence of an authorized generic causes generic prices to be more than 15% lower than when there is no authorized generic. IMS Consulting, *Assessment of Authorized Generics in the U.S.* (2006).

[32] One generic company stated that "[d]ue to market share and pricing erosion at the hands of the authorized [generic], we estimate that the profits for the 'pure' generic during the exclusivity period could be reduced by approximately 60% in a typical scenario." *See* FTC 2011 AG Study at 81. Another generic manufacturer quantified the market consequences of competing with an authorized generic and determined that the authorized generic reduced its first generic's revenues by two-thirds, or by approximately $400 million. Comment of Apotex Corp. in Support of Mylan Citizen Petition at 4, Docket No. 2004P-0075 (Mar. 24, 2004), available at https://paragraphfour.com/uploads/educ/2004P0075Apotex.pdf (last accessed August 21, 2024).

[33] Commenting on an FDA petition by generic drug manufacturer Teva Pharmaceuticals, Pfizer stated: "Teva's petition [to prevent the launch of an authorized generic] is a flagrant effort to stifle price competition – to Teva's benefit and the public's detriment." Comment of Pfizer at 6- 7, Docket No. 2004P-0261 (June 23, 2004); Comment of Johnson & Johnson at 1, FDA Docket No. 2004P-0075 (May 11, 2004).

there was no viable basis upon which to seek patent protection for the pomalidomide uses and formulations.

1. Thalidomide and its analogs, including pomalidomide.

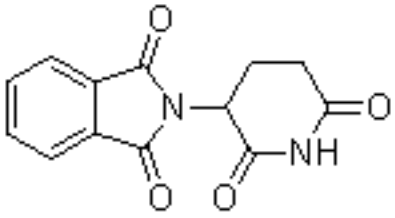
63. During the drug development process, once a promising compound is identified, scientists investigate both its properties and its analogs. An analog is a compound with similar chemical structure but differing in more than one respect.

64. Immunomodulatory drugs (IMiDs) are drugs that adjust immune responses. IMiDs also have anti-angiogenic effects, meaning they inhibit the ability of a tumor to grow its own blood vessels.

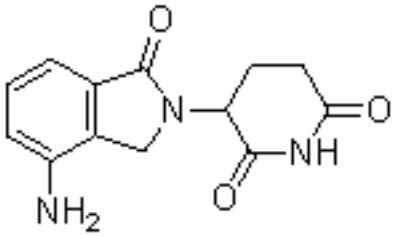
65. The ImiD class includes thalidomide and its analogs lenalidomide and pomalidomide.

66. This case involves wrongdoing regarding pomalidomide, the third of the thalidomide compounds to be marketed in the United States (the first being thalidomide, the second lenalidomide). Although pomalidomide was the third IMiD to be *marketed* in the United States, fundamental research for the use of thalidomide and its analogs, including pomalidomide and lenalidomide, to treat various conditions including multiple myeloma, occurred *concurrently*.

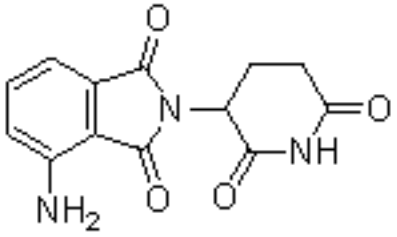
67. The chemical structure of thalidomide is:



68. The chemical structure of lenalidomide is:

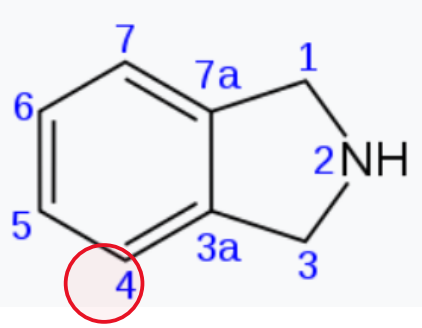


69. The chemical structure of pomalidomide is:



70. During research of a chemical compound, the drug is typically referred to by its chemical name. Because chemical names are often complex and cumbersome for general use, a shorthand version of the chemical name or a code name (such as CI 981) is developed for easy reference among researchers, and internally at a company there may be other code names. If the drug is eventually approved by the FDA, the compound is given an official generic name (such as bupropion) and a brand name (such as Wellbutrin). In the United States, the United States Adopted Names (USAN) Council assigns generic names.

71. The chemical name of pomalidomide is 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione. During research of the compound at issue in this case, the drug was at times referred to with the shortened chemical name "3-aminothalidomide" and at later times as "4-aminothalidomide". The leading number reflects the position on the isoindoline ring where the amino group ("NH2") connects. Whether the initial number for pomalidomide is considered "3" or "4" depends on where on the isoindoline ring the chemist begins counting. The numbering, subject to the naming conventions of the International Union of Pure and Applied Chemistry (IUPAC), changes based on which carbon the amino group is attached to. It is a uniform way for scientists to understand the compound of the structure.

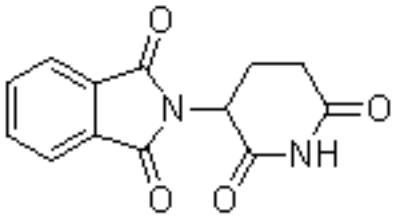
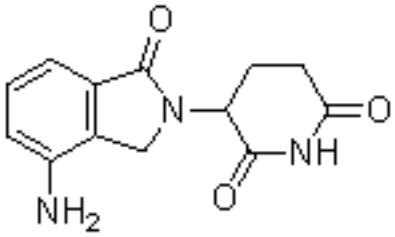
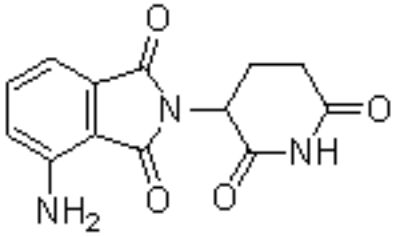
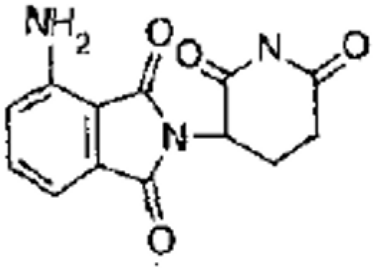


72. The point on the isoindoline ring above labeled as the "4 position" would instead be the "3 position" if the chemist began counting one position to the right (where the NH group attaches).

73. For pomalidomide, original studies described the amino group as attached to carbon 3 of the isoindoline ring and was referred to as "3-aminothalidomide." Later studies described the amino group as attached to carbon 4 of the isoindoline ring and referred to as "4-aminothalidomide." While careful review of diagrams can show whether it is, or is not, depicting the same molecule, inconsistent use of differing terms can lead to confusion. As detailed below, Celgene exploited this potential for confusion during its patent prosecution designed to elongate market exclusivity for Pomalyst.

74. Pomalidomide also had several other short-hand names, including ACTIMID and CC-4047. Eventually, the common generic name for the compound became "pomalidomide." This Complaint applies the term "pomalidomide" to circumstances prior to when the drug was given that official name, except when quoting others that used a different moniker.

75. The below table summarizes the chemical and other names ascribed to thalidomide, lenalidomide, and pomalidomide.

Compound	Drawing	Chemical Name	Other Names
thalidomide (in Thalomid)		2-(2,6-dioxopiperidin-3-yl-1H-isoindole-1,3(2H)-dione	
lenalidomide (in Revlimid)		1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline	Revlimid; CC-5013
Pomalidomide (in Pomalyst)	 CAN ALSO BE DRAWN: 	1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline. 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione	3-aminothalidomide; 4-aminothalidomide; ACTIMID; CC-4047; CDC 394; S-3-Amino-phthalimido-glutarimide

2. 1960s to 1990s—the study of thalidomide and its analogs.

76. Thalidomide gained international attention in the 1960s. It was often prescribed to pregnant women to treat morning sickness. But it soon became understood that thalidomide, when taken during a critical phase of pregnancy, could cause severe birth defects, primarily resulting in the malformation or absence a limb of the unborn children. Substances that interfere with normal fetal development and/or cause congenital disabilities are referred to as "teratogens" or "teratogenic."

77. Once thalidomide's teratogenic properties were discovered, in 1961, the drug was banned. Indeed, the thalidomide fiasco is often attributed as leading to major reforms in U.S. drug approval process.

78. Several years after thalidomide was withdrawn from the market for its propensity to induce severe birth defects, another innocuous use was attributed to the drug. Thalidomide's anti-inflammatory properties helped patients with erythema nodosum leprosum (ENL), a condition associated with leprosy[34] who used the drug as a sedative by reducing both the clinical signs and symptoms of the disease.

79. The discovery of the anti-angiogenic and anti-inflammatory properties of thalidomide would lead to the development of analogs of thalidomide as a new way of fighting cancer as well as some inflammatory diseases. The thesis was that analogs of thalidomide might be more effective and/or safer, and reduce thalidomide's teratogenic side effects, high incidence of other adverse reactions, poor solubility in water, and poor absorption from the intestines.

80. Pomalidomide was one of thalidomide's analogs that showed promising properties. As early as 1965, pomalidomide was known to be an analog of thalidomide that caused dysmelia: *i.e.*, malformation of limbs and extremities.[35] By the 1970s and early 1980s, pomalidomide's causal relationship to other, similar birth defects expanded.[36]

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[34] *See* Teo S, Resztak KE, Scheffler MA, Kook KA, Zeldis JB, Stirling DI, Thomas SD., *Thalidomide in the treatment of leprosy.* Microbes Infect. 2002 Sep;4(11):1193-202. doi: 10.1016/s1286-4579(02)01645-3. PMID: 12361920. (stating that thalidomide has been used to treat ENL since the 1960s), available at https://pubmed.ncbi.nlm.nih.gov/12361920/sd (last accessed August 21, 2024).

[35] *See* R.L. Smith, et al., *Studies on the Relationship Between the Chemical Structure and Embryotoxic Activity of Thalidomide and Related Compounds*, A Symposium on Embryopathic Activity of Drugs, London (1965).

[36] *See* H. Koch, *The Arene Oxide Hypothesis of Thalidomide Action - Considerations on the Molecular Mechanism of Action of the Classic Teratogen*, sci. phann., p. 49, 67—99 (1981); N.A. Jonsson, *Chemical Structure and teratogenic properties*, acta pharm. Succica, 9:521—542 (1972).

81. In the early 1990s, multiple studies reported that thalidomide inhibited tumor necrosis factor-alpha (TNFα).[37] In healthy people, TNFα helps the immune system fight infections and kills tumor cells. It encourages modest inflammation, which helps the body heal. In patients with autoimmune conditions, however, TNFα can cause excessive inflammation and worsen symptoms.

82. TNFα is a cytokine—a type of signaling molecule in the immune system—produced by various cells, such as macrophages, in response to infection, injury, or other inflammatory stimuli. While TNFα plays a crucial role in salubrious inflammation and immune response, elevated amounts of TNFα are associated with a few diseases, including cancer.[38] At that time, scientists were investigating whether thalidomide-like compounds could reduce TNFα, and if they could be used to treat cancer or autoimmune conditions.

83. The renewed interest in thalidomide to treat a host of diseases, including cancer, extended beyond the scientific community, and was reported widely in the media.[39] And so, by the

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[37] Sampaio, Sarno, Galilly Cohn and Kaplan, JEM 173 (3) 699–703, 1991; Sampaio EP, Kaplan G, Miranda A, Nery J.A., Miguel CP, Viana SM, Sarno EN. *The influence of thalidomide on the clinical and immunologic manifestation of erythema nodosum leprosum*. J Infect Dis. 1993 Aug;168(2):408-14. doi: 10.1093/infdis/168.2.408. PMID: 8335978 ("Patients with systemic ENL demonstrated the highest serum TNF alpha levels, which decreased significantly during thalidomide treatment.").

[38] De SK, Devadas K, Notkins AL. Elevated levels of tumor necrosis factor alpha (TNF-alpha) in human immunodeficiency virus type 1-transgenic mice: prevention of death by antibody to TNF-alpha. J Virol. 2002;76(22):11710-11714. doi:10.1128/jvi.76.22.11710-11714.2002 ("Elevated levels of circulating TNF-α have been linked to a wide variety of diseases, including arthritis, diabetes, Crohn's disease, and cachexia associated with terminal cancer and AIDS."), available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC136749/#:~:text=Elevated%20levels%20of%20circulating%20TNF,cancer%20and%20AIDS%20(23) (last accessed August 21, 2024).

[39] *See, e.g.*, Lawrence Altman, *Researchers Testing Thalidomide for Use in AIDS,* N.Y. Times (July 1, 1993) ("Thalidomide works in laboratory experiments against H.I.V. by selectively suppressing a natural substance produced in the body, the authors reported in the Proceedings of the National Academy of Sciences. The substance, tumor necrosis factor, also called cachectin, defends against infection, and it has been the subject of intense research in

early 1990s, multiple research groups across the country were studying the use of thalidomide and its analogs to treat cancers, AIDs, and other conditions.

3. 1990s: D'Amato and Boston Children's Hospital's investigations and patents.

84. In the 1990s, researchers at Children's Hospital in Boston were investigating whether they could slow tumor growth by cutting off or restricting blood flow to the area surrounding the tumor. These investigators hypothesized that solid tumors require angiogenesis, or the development of blood vessels, for their growth and persistence. At least as early as 1992, one of the researchers, Dr. Robert D'Amato, began a search for compositions that would inhibit undesired angiogenesis in humans and animals. After careful testing, D'Amato discovered that thalidomide inhibits angiogenesis (is "anti-angiogenic").

85. Once D'Amato and others discovered thalidomide's anti-angiogenic properties, they began investigating whether it and its analogues could be used to treat conditions associated with angiogenesis, such as cancers, blood cancers, tumors, arthritis, and autoimmune conditions.

86. Over the next decade, D'Amato and other researchers at Boston's Children's Hospital extensively studied the properties and uses of thalidomide, lenalidomide, pomalidomide, and many other analogues. In the course of this study, they amassed a large portfolio of intellectual property touching on the iMIDs.

87. For example, a series of patent applications (starting with a priority date of March 1, 1993) disclosed that thalidomide and other analogs, including lenalidomide and pomalidomide, were

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cancer and many other diseases."), available at https://www.nytimes.com/1993/07/01/us/researchers-testing-thalidomide-for-use-in-aids.html (last accessed August 21, 2024).

See also Sandra Blakeslee, *Scorned Thalidomide Raises New Hopes,* N.Y. Times (Apr. 10, 1990), available at https://www.nytimes.com/1990/04/10/science/scorned-thalidomide-raises-new-hopes.html (last accessed August 21, 2024); *see also* Washington Post (Apr. 11, 1991), *Drug Firms Seek to Make Thalidomide for Research,* available at https://www.washingtonpost.com/archive/politics/1991/04/11/drug-firms-seek-to-make-thalidomide-for-research/bead3a71-7d37-4948-a917-eb8c0aa253b2/ (last accessed August 21, 2024).

useful in treating numerous diseases mediated by angiogenesis, such as cancer, both blood-born and solid tumors, chronic inflammation, such as rheumatoid arthritis and osteoarthritis, and other inflammatory diseases, such as ulcerative colitis and Crohn's disease. The patent applications disclosed suitable routes for administration of the active ingredients. The applications stated that, "angiogenesis inhibition is generally an important mechanism for the operation of teratogenic compounds (particularly compounds that cause dysmelia; *i.e.*, malformation of limbs and extremities). Such anti-angiogenic compounds generally can be used to treat diseases characterized by undesired angiogenesis."

88. In 1994, Dr. D'Amato published an article explaining how thalidomide was found to have anti-angiogenic activity.[40]

89. In addition to testing thalidomide's effect on angiogenesis, D'Amato tested other compounds, including pomalidomide, which he routinely referred to as "3-amino thalidomide". During the 1990s, D'Amato obtained several patents claiming or teaching the use of 3-amino thalidomide (*i.e.*, pomalidomide) as a method of treating undesired angiogenesis in a human or animal. Those patents include numbers 5,593,990 ('990), 5,629,327 ('327), and 5,712,291 ('291) ("the D'Amato patents").

90. D'Amato's research into thalidomide and its analogs and his growing patent portfolio began to threaten Celgene's investigations in the same area. D'Amato's research pre-dated that of Celgene's, thus presenting a body of prior art that would undermine Celgene's attempts to patent the same thalidomide analogs.

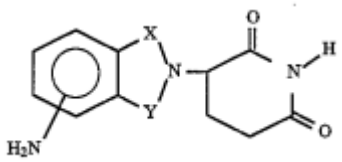
[40] D'Amato RJ, Loughnan MS, Flynn E, Folkman J (April 1994), *Thalidomide is an inhibitor of angiogenesis,* Proc. Natl. Acad. Sci. U.S.A. 91 (9): 4082. ("D'Amato 1994").

4. 1990s: Celgene's investigations and the '517 patent.

91. At the same time as D'Amato's research efforts, during the 1990s, Celgene researchers also explored the development of thalidomide and its analogs for their anti-angiogenic and anti-myeloma activities.

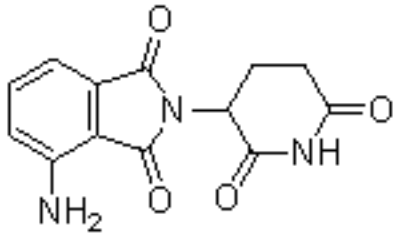
92. On July 24, 1996, Celgene[41] filed patent application no. 08/690,258, which led to U.S. Patent No. 5,635,517 (the "'517 patent"). The '517 patent identified thalidomide analogs, including lenalidomide and pomalidomide, as compounds decreasing TNFα levels. As the '517 patent explains, "[d]ecreasing TNFα levels . . . constitutes a valuable therapeutic strategy for the treatment of many inflammatory, infectious, immunological or malignant diseases. . . . These include but are not limited to . . . cancer . . . ."

93. The '517 patent has two independent claims (Claim 1 and 10). Claim 1 claims:

> "The method of reducing undesirable levels of TNFα in a mammal which comprises administering thereto an effective amount of a compound of the formula:
>
> 
>
>
> in which said compound one of X and Y is C=O and the other of X and Y is C=O or CH."

94. One variation encompassed by Claim 1 is a method of reducing TNFα with a compound of the structure depicted above, where X and Y both have a carbon atom double bonded to an oxygen atom (represented above as "C=O"). As shown below, this is pomalidomide:

[41] The inventors on the patent are listed as George Muller, David Stirling, and Roger S.C. Chen., all of whom worked for Celgene. The assignee of the patent is Celgene Corporation. Because the inventors were affiliated with Celgene, and Celgene was the assignee of the patent when issued, the Complaint refers to the patent applicant as "Celgene." This convention is also used when referencing the relevant patent prosecutions.



95. Claim 7, a dependent claim, claims this specific variation in the formula, that is, "The method according to claim 1 in which each of X and Y is C=O."

96. Claim 8—also a dependent claim—claims "The method according to claim 7 in which said compound is 1,3-dioxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline." This is the chemical name for pomalidomide.

97. Taken together, Claims 1, 7, and 8 of the '517 claim methods of using pomalidomide to reduce TNFα. The '517 patent does not claim the compound pomalidomide by itself; the claim in the '517 patent that claims a compound by itself is Claim 10 which does claim four compounds, but none are pomalidomide.

98. Thus, as early as 1996, Celgene owned a patent that claimed a method of using pomalidomide to reduce TNFα, which the '517 discloses is "a valuable therapeutic strategy for the treatment of. . . . cancer. . . ."[42]

99. The '517 patent also claims the compound lenalidomide (*i.e.*, Revlimid) and methods of using lenalidomide to reduce undesirable levels of TNFα. The '517 patent would later become the foundation of Celgene's Revlimid franchise, earning it $35 billion in the U.S. in the last five years alone. Revlimid, in combination with the steroid dexamethasone, is used primarily in the treatment of multiple myeloma, a blood cancer.

[42] *See* the '517, column 3, lines 59–67.

5. 1990s: Celgene hired Dr. Jerome B. Zeldis and Anthony Insogna.

100. In or about 1996, Celgene first retained Anthony Insogna. At the time, Insogna was a patent attorney at the New York law firm of Pennie & Edmonds. Insogna worked at Pennie & Edmonds on behalf of Celgene for years, with an emphasis on intellectual property protection for ostensible inventions relating to thalidomide and its analogs. In 2003, Insogna became employed by the law firm Jones Day, and continued his work for Celgene.

101. Also, in the 1990s Celgene hired Dr. Jerome B. Zeldis. Zeldis joined Celgene in 1997 as Vice President of Medical Affairs. Zeldis has a scientific background and holds an MD and a PhD in Molecular Biophysics and Biochemistry. In 1999, Zeldis was named Chief Medical Officer at Celgene, where he was responsible for identifying new disease targets for Celgene's drugs and crafting studies and clinical trials to support Celgene's New Drug Applications.

102. As shown below, both Insogna and Zeldis, through their work with Celgene, had personal and significant knowledge regarding public disclosures and prior art, predating late 2002, regarding pomalidomide and its uses and formulation.

6. 1998-2002: Reissuance proceedings for the '517 patent show knowledge of pomalidomide and its properties.

103. In early 1998, Celgene realized that the '517 patent, the keystone of its thalidomide analog patents, might be invalid due to earlier patents granted to D'Amato and other Children's Hospital researchers.

104. On April 14, 1998, Celgene sought reexamination of the '517 to clear it from the specter of the potentially invalidating D'Amato patents.

105. In December 1998, Celgene entered into a license agreement with Children's Hospital (and its development partner, Entremed) under which Celgene bought some license rights to the early D'Amato patents.

106. Celgene's effort to clear the '517 backfired. On February 21, 1999, the PTO rejected all claims of the '517 as unpatentable over the three D'Amato patents (the 5,593,990, 5,629,327, and 5,712,291) and in view of the two other references.[43] In explaining its determination that the claims were unpatentable as obvious, the PTO stated: "the record has shown and the patentee has admitted in the record that the 3 D'Amato patents contain the same disclosure and said D'Amato patents supra disclose the very closely analogous compounds, . . .and methods for their preparation." The examiner further stated that the record showed that "[the] concept of angiogenesis and administering said reference compounds to a patient with toxic concentrations of TNF-α is taught [in the D'Amato patents]." The examiner thus concluded that, "[s]ince the properties of the prior art overlap with the ['517] under reexamination, and the 3-D'Amato patents teach the equivalents . . . there is ample information in the prior [art] to motivate one of ordinary skill in the chemical arts to place applicants [sic] compounds in possession of the public."

107. In February 1999, Celgene filed for reconsideration and presented a declaration by its then-Chief Scientific Officer, David I. Stirling to the PTO in primary support thereof. The data described by Stirling purported to show that "Compound 2" (which in fact was pomalidomide) was 10,000-fold more active than another compound (4-hydroxythalidomide) in the primary human cell-based assay.

108. Celgene's representations in its reconsideration request both vastly exaggerated the extent to which "Compound 2" outperformed the other chemical, and misleadingly suggested "Compound 2" was lenalidomide (when in fact it was pomalidomide). Instead, the reexamination proceedings show that it was public knowledge that careful review of the '517 patent revealed that it

[43] U.S. Patent No.4,808,402 (Leibovich is a named inventor) and Leibovich et al., *Macrophage-Induced Angiogenesis is Mediated Tumor Necrosis factor-a*, Letters To Nature, Vol.329, 630─32, (filed Oct. 15, 1987).

claimed methods of using pomalidomide, and that pomalidomide had been tested as a powerful thalidomide analog in inhibiting TNFα.

109. On March 9, 1999, the patent examiner issued a Statement of Reasons for Patentability and/or Confirmation that allowed the patent to re-issue because the examiner believed the "claimed compound" was shown to be superior:

> The data presented in the Dr. David I. Sterling [sic] Declaration, kindly furnished under the provisions of 37 C.F.R. 1.132 clearly shows unexpected superior results when the claimed compound, namely, 7-amino-1-oxo-2(2,6-dioxo-piperidin-3-yl)-isoindoline,[44] when compared to the corresponding 7-hydroxy -1-oxo-2(2,6-dioxo-pi_peridin-3-yl)-isoindoline of the prior art in a side-by-side comparison. . . . Looking at the data, the claimed compound is clearly superior in the inhibition of TNF-alpha (Tumor Necrosis Factor) at concentration levels IC_{50}.

110. Although Celgene ultimately managed to convince the examiner to reissue the '517, Celgene was on notice and could no longer ignore that there was broad, public information about (i) thalidomide analogs, (ii) the relative activities of the analogs could vary widely, and (iii) that effectiveness of pomalidomide had now been publicly disclosed by Celgene itself.

7. 1998: Celgene seeks a leprosy-related indication for thalidomide.

111. Meanwhile, Celgene had been pursuing FDA approval of thalidomide to treat erythema nodosum leprosum (ENL).

112. On July 15, 1998, the FDA approved Celgene's new drug application for thalidomide 50 mg for the acute treatment of the cutaneous manifestations of moderate to severe ENL. While the approved indication was for ENL, given increasing scientific research showing the ability of

[44] "7-amino-1-oxo-2(2,6-dioxo-piperidin-3-yl)-isoindoline" corresponds to the fourth compound claimed in Claim 10 of the '517, *i.e.* 1-oxo-2-(2,6-dioxopiperidin-3-yl)-7aminoisoindoline. The patent examiner most likely meant Compound 2 (which is pomalidomide in the Sterling declaration) when he referenced 7-amino-1-oxo-2(2,6-dioxo-piperidin-3-yl)-isoindoline. The Sterling declaration makes no mention of 7 aminoinoisindoline. The declaration, however, states that Compound 2 is clearly superior in the inhibition of TNF-alpha.

thalidomide (and its analogs) to inhibit TNFα and its effect on multiple myeloma, over time (before the 2006 formal approval for multiple myeloma) thalidomide was used off-label to treat multiple myeloma.

113. Multiple myeloma is a cancer that forms in plasma cells. Plasma cells are a type of white blood cell. In healthy individuals, plasma cells help fight infections by making antibodies. In multiple myeloma patients, cancerous plasma cells build up in the bone marrow and crowd out the healthy blood cells.

114. Following the approval of thalidomide for ENL, the scientific community continued to report on thalidomide analogs, such as pomalidomide, including regarding their effect on multiple myeloma, relative potency, and the ability of thalidomide analogs (such as lenalidomide and pomalidomide) to treat relapsed or refractory disease.

115. For example, on June 7, 1999, the journal of Bioorganic & Medicinal Chemistry Letters published a study by G.W. Muller and others ("Muller (1999)")[45] disclosing the structure of pomalidomide and teaching that "4-amino substituted analogs were found to be potent inhibitors of TNF-α." On July 1, 1999, the Journal of Immunology likewise published a study by L.G. Corral and others ("Corral (1999)")[46] teaching pomalidomide[47] as a more potent agent with decreased potential for birth defects. In 2000, the influential American Society of Hematology journal Blood published a

[45] Muller GW, Chen R, Huang SY, Corral LG, Wong LM, Patterson RT, Chen Y, Kaplan G, Stirling DI. *Amino-substituted thalidomide analogs: potent inhibitors of TNF-alpha production.* Bioorg Med Chem Lett. 1999 Jun 7;9(11):1625-30. doi: 10.1016/s0960-894x(99)00250-4. PMID: 10386948, available at https://www.sciencedirect.com/science/article/abs/pii/S0960894X99002504?via%3Dihub (last accessed August 21, 2024).

[46] Corral LG, Haslett PA, Muller GW, Chen R, Wong LM, Ocampo CJ, Patterson RT, Stirling DI, Kaplan G. *Differential cytokine modulation and T cell activation by two distinct classes of thalidomide analogues that are potent inhibitors of TNF-alpha.* J Immunol. 1999 Jul 1;163(1):380-6. PMID: 10384139, available at https://pubmed.ncbi.nlm.nih.gov/10384139/ (last accessed August 21, 2024).

[47] Pomalidomide is referred to in the study as "compound CI-A."

study by Hideshima and others ("Hideshima (2000)") regarding the ability of thalidomide and its analogs to overcome drug resistance of multiple myeloma cells.[48]

8. 2000-2002: Celgene applies for and obtains the '230 and '554 patents, both disclosing that pomalidomide can be used to reduce TNFα.

116. On April 6, 2000, Celgene filed a patent application (in the '517 family) that led to the 6,281,230 (issued in 2001). The '230 claims methods of treatment involving lenalidomide to treat cancerous conditions and reduce TNFα. It also disclosed pomalidomide in combination with an active agent as part of the '230 methods of treatment claims.

117. On February 12, 2001, Celgene filed a patent application (again in the '517 family) that led to the 6,555,554 (issued in 2003). The '554 claimed methods of treatment involving lenalidomide to improve oncogenic or cancerous conditions and reduce TNFα. As with the '230, the '554 also disclosed pomalidomide in its methods of treatment claims.

118. Like the '517, the '230 and the '554 patents both publicly disclosed that pomalidomide can be used to reduce TNFα.

9. 2000-2002: Scientists continue to publish about pomalidomide's features and benefits.

119. The scientific community continued to study and publish on the potency of thalidomide analogs and the use of thalidomide in combination with dexamethasone to treat multiple myeloma.

[48] Teru Hideshima, Dharminder Chauhan, Yoshihito Shima, Noopur Raje, Faith E. Davies, Yu-Tzu Tai, Steven P. Treon, Boris Lin, Robert L. Schlossman, Paul Richardson, George Muller, David I. Stirling, Kenneth C. Anderson; *Thalidomide and its analogs overcome drug resistance of human multiple myeloma cells to conventional therapy*. Blood 2000; 96 (9): 2943–2950. doi: https://doi.org/10.1182/blood.V96.9.2943 (last accessed August 21, 2024).

120. For example, Weber and others ("Weber 2000")[49] disclosed the clinical efficacy of thalidomide with dexamethasone to treat resistant multiple myeloma.

121. On July 1, 2001, Blood also published a study by Davies and others ("Davies 2001"),[50] which disclosed that thalidomide and immunomodulatory drugs (referred to in the study as IMiD1, IMiD2, and IMID3) act directly on multiple myeloma cells and are useful in relapsed/refractory disease. Davies 2001 further disclosed that the new thalidomide analogs are 50,000 times more potent in inhibiting TNFα than thalidomide. As explained above, "IMiDs" was a term coined by Celgene, referring most prominently to pomalidomide and lenalidomide.

122. On December 1, 2001, Robert A. Kyle and others ("Kyle (2001)")[51] published an article disclosing a method of treating multiple myeloma by administering thalidomide in combination with dexamethasone cyclically.

123. Also in December 2001, Dimopoulos and others ("Dimopolous (2001)")[52] disclosed that thalidomide plus dexamethasone can usefully treat refractory multiple myeloma.

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[49] Weber, et al., Abstract #719, *Thalidomide with dexamethasone for resistant multiple myeloma*, Blood, 96(11):167a (2000)

[50] Davies FE, Raje N, Hideshima T, Lentzsch S, Young G, Tai YT, Lin B, Podar K, Gupta D, Chauhan D, Treon SP, Richardson PG, Schlossman RL, Morgan GJ, Muller GW, Stirling DI, Anderson KC. *Thalidomide and immunomodulatory derivatives augment natural killer cell cytotoxicity in multiple myeloma.* Blood. 2001 Jul 1;98(1):210-6. doi: 10.1182/blood.v98.1.210. PMID: 11418482, available at https://pubmed.ncbi.nlm.nih.gov/11418482/ (last accessed August 21, 2024).

[51] Kyle, Robert A, and S.Vincent Rajkumar. *Therapeutic Application of Thalidomide in Multiple Myeloma.* Seminars in Oncology 28, no. 6 583–87 (Dec. 1, 2001) doi:10.1016/S0093- 7754(01)90028- 4, summary available at https://journals.scholarsportal.info/details/00937754/v28i0006/583_taotimm.xml (last accessed August 21, 2024).

[52] Dimopoulos and others, et al., *Thalidomide and dexamethasone combination for refractory multiple myeloma*, Ann. Oncology, 12-991-995 (2001)

124. The prior art also disclosed the specific amount of 40 mg of dexamethasone plus thalidomide for the treatment of multiple myeloma.[53]

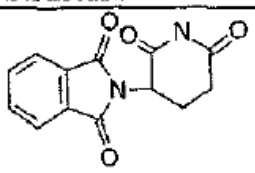
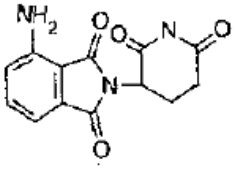
125. These disclosures regarding the use of thalidomide in combination with 40 mg of dexamethasone to treat multiple myeloma were additive to the much earlier disclosures regarding the cyclical dosing of an anticancer drug (hexamethylamine) for the treatment of multiple myeloma, *i.e.,* 21 consecutive days of administration of the anticancer drug followed by 7 days of rest, in combination with dexamethasone.[54]

126. The prior art also taught the specific thalidomide analog pomalidomide for the treatment of multiple myeloma. In December 2001, D'Amato and others published an article entitled *Mechanisms of Action of Thalidomide and 3-Aminothalidomide in Multiple Myeloma* (the "D'Amato (2001)").[55] The title refers to "3-aminothalidomide," and a diagram in the article (among other evidence) makes clear that the compound discussed in the study is pomalidomide:

[53] *See* Coleman, et al., *BLT-D (Clarithrmycin [Biaxin], Low-Dose Thalidomide, and Dexamethasone) for the Treatment of Myeloma and Waldenstroms Macroglobulinemia*, Leukemia & Lymphona, 43(9):1777—1782 (2002).

[54] *See* Cohen, et al., *Hexamethylamine and prednisone in the treatment of refractory multiple myeloma*, Am. J. Clin. Oncol. (CCT), 5:21—27 (Feb. 1982).

[55] Robert J D'Amato, Suzanne Lentzsch, Kenneth C Anderson, Michael S Rogers, *Mechanism of action of thalidomide and 3-aminothalidomide in multiple myeloma*, Seminars in Oncology, Volume 28, Issue 6, 2001, 597–601, ISSN 0093-7754, https://doi.org/10.1016/S0093-7754(01)90031-4 (last accessed August 21, 2024).

Compound	Structure	bFGF Inhibition	VEGF Inhibition
Thalidomide		39%	41%
3-Aminothalidomide		30%	42%

127. This reference taught pomalidomide for the treatment of multiple myeloma, stating that pomalidomide "exhibited an unusual capacity to directly inhibit myeloma proliferation." It noted that pomalidomide directly inhibited myeloma cell proliferation and thus inhibited multiple myeloma both on the tumor and vascular compartments. The dual activity of pomalidomide was reported to make it more efficacious than thalidomide both *in vitro* and *in vivo*.[56] This effect was reported to be unrelated to TNFα inhibition since potent TNFα inhibitors such as rolipram and pentoxifylline did not inhibit myeloma cell growth or angiogenesis.[57]

128. Also in December 2001, Lentzsch and others ("Lentzsch (2001)")[58] disclosed that pomalidomide (referred to in the article as S-3-Amino-phthalimido-glutarimide or S-3APG for short) has notable anti-multiple myeloma activity, concluding that "[o]ur results show that S-3APG could be a potent new drug for the treatment of MM. S-3APG exerts its anti-myeloma activity by

[56] Lentzsch S, Rogers MS, LeBlanc R, et al. (Apr. 2002). *S-3-Amino-phthalimido glutarimide inhibits angiogenesis and growth of B-cell neoplasias in mice.* Cancer Res. 62 (8): 2300–5. PMID 11956087.

[57] D'Amato RJ, Lentzsch S, Anderson KC, Rogers MS (Dec. 2001). *Mechanism of action of thalidomide and 3-aminothalidomide in multiple myeloma.* Semin. Oncol. 28 (6): 597–601. doi:10.1016/S0093-7754(01)90031-4. PMID 11740816.

[58] Lentzsch et al., Abstract #1976, *S-3-Amino-phthalimido-glutarimide Inhibits Growth in Drug Resistant Multiple Myeloma (MM) In Vivo,* Blood, 43rd Annual Amer. Soc. Hematol. (Dec. 7-11, 2001), 98(11): 473a (2001).

combination of direct dose-dependent anti-proliferative effect on MM cell lines resistant to conventional therapy and by inhibition of angiogenesis in vivo. Thus, S-3-APG demonstrates superior *in vivo* anti-MM-activity compared to Thal and induces sustained complete tumor remission *in vivo*, without evidence of toxicity."

129. In April 2002, Lentzsch and others published ("Lentzsch 2002")[59] which taught that pomalidomide was able to directly inhibit the proliferation of myeloma and that pomalidomide is "a powerful anti-myeloma and anti-B-cell-lymphoma agent that has both antiproliferative and antiangiogenic effects."

130. Also in April 2002, Schey and others ("Schey (April 2002)")[60] disclosed pomalidomide (referred to in the article as CC4047) for the treatment of multiple myeloma in humans. Schey (April 2002) further disclosed "Phase I dose escalation study in relapsed/refractory multiple myeloma designed to identify the maximum tolerated dose (MTD) and evaluate the safety of CC-4047 when given orally for 4 weeks. Patients were enrolled in cohorts of 3 at each dose level: 1mg/day, 2mg/d, 5mg/d and 10mg/d." Schey (April 2002) established the maximum tolerated dose at 5 mg/day.

131. In October 2002, Schey, S.A. published an article, ("Schey (October 2002)")[61] that disclosed a phase I study of pomalidomide (again referred to in the study as CC-4047) in relapsed and refractory multiple myeloma.

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[59] Lentzsch et al., *S-3-Amino-phtahlimido-glutarimide Inhibits Angiogenesis and Growth of B-Cell Neoplasias in Mice,* Cancer Research, 62:2300-2305 (2002).

[60] Schey et al., Abstract #248, *A Phase I Study of an Immunomodulatory Thalidomdie Analogue (CC4047) in Relapse/Refractory Multiple Myeloma,* Experimental Hematology (31st Annual Meeting of the International Society for Experimental Hematology) (July 5-9, 2002).

[61] Schey, S.A. *Thalidomide in the management of multiple myeloma,* Hematology 7(5):291-299 (October 2002).

132. Despite the use of different terms and nomenclature, these early 2000s publications teach pomalidomide to treat multiple myeloma. They are potentially invalidating prior art for anyone, including Celgene, who tried to patent pomalidomide as a compound or as a method to treat multiple myeloma. And indeed, many of these studies were roadblocks for Celgene's Pomalyst patents.

133. Meanwhile, Celgene had continued publication of pomalidomide findings.

134. For example, on November 13, 2001, the PTO issued U.S. Patent No. 6,316,471 ("the '471 patent") entitled "Isoindolines, Method of Use, and Pharmaceutical Compositions" to Celgene. Celgene would later list this patent in the Orange Book for Pomalyst. The '471 patent teaches the use of certain compounds including pomalidomide in the treatment of autoimmune diseases and cancers. The '471 patent also discloses that pomalidomide can be administered orally to reduce TNFα and can be administered in the form of a capsule or tablet containing from 1 to 100mg of drug per unit dosage. The '471 patent discloses that decreasing TNFα constitutes a valuable therapeutic strategy to treat cancer. Claim 1 is directed to methods of treatment using pomalidomide and claim 16 is directed to the use of pomalidomide to treat an oncogenic or cancerous condition. The '471 patent also teaches that pomalidomide and lenalidomide can be administered in combination with other active compounds, including antibiotics and steroids, such as dexamethasone.

135. When the '471 patent issued, Celgene announced that the patent claims covered "the use of ACTIMID™ (CDC 394), Celgene's next IMiD™, to treat cancer and inflammatory diseases both as a single agent and in combination with other therapies."[62] ACTIMID is pomalidomide.

[62] *See* Celgene Press Release (Nov. 13, 2001).

10. 2002: Celgene's need to buy technologies owned by Boston Children's Hospital.

136. By 2002, the D'Amato team at Children's Hospital had developed its thalidomide analog portfolio of intellectual property. And its development partner, EntreMed, had planned Phase I clinical trials for pomalidomide (the first step in seeking FDA approval to market a prescription drug). D'Amato had also pursued further patents. By mid-2002, some of those issued-patents and patent applications were for compositions and methods of using pomalidomide.[63] Particularly, pomalidomide had been shown to induce sustained tumor regression in multiple myeloma, and to do so even in tumors from cell lines resistant to conventional chemotherapy.

137. Threatened by the progress of the D'Amato/EntreMed drug development program, according to a complaint filed by Entremed, Celgene "embarked on an intentional campaign to harm EntreMed" and "to monopolize the market for aminothalidomide drugs by preventing innovation competition between EntreMed and Celgene."[64] Celgene, in turn, sued EntreMed and the PTO, asking the Court to enjoin the PTO from issuing more thalidomide analog patents to EntreMed's development partner, Dr. D'Amato.[65] EntreMed sued Celgene for antitrust violations based on Celgene's alleged interference with EntreMed's efforts to develop thalidomide analogs to treat cancer.[66] In this litigation, Celgene was represented by Anthony Insogna's law firm at the time, Pennie & Edmonds.

138. On December 31, 2002, EntreMed and Celgene settled and entered into a three-way licensing agreement that included Children's Hospital. The license agreement specifically had

[63] U.S. patent no. 5,593,990 (issued Jan. 14, 1997); U.S. patent no. 5,712,291 (issued Jan. 27, 1998); patent application no. 09/899,344 (filed July 5, 2001); patent application no. 10/020,391 (filed Dec. 12, 2001).

[64] *EntreMed, Inc. v. Celgene*, 02-3787 (D. Md.), Complaint at ¶ 13 (filed Nov. 21, 2002).

[65] *Celgene Corp. v. James E. Rogan, et al.,* case no. 02-cv-2277 (D.D.C.) (filed Nov. 19, 2002).

[66] *EntreMed, Inc. v. Celgene,* 02-3787 (D. Md.) (filed Nov. 21, 2002).

different definitions for "Amino Thalidomide" using the chemical structure diagram for pomalidomide and "Revimid" using the chemical structure diagram for lenalidomide. In exchange for future royalties, "Children's would grant Celgene an exclusive license to patents and patent applications . . . in consideration of Celgene's payment of specified payments, including but not limited to running royalties on Amino Thalidomide and Revlimid products."[67]

139. Under the arrangement, Celgene became the exclusive licensee for a broad portfolio of pending patent applications and published patents—all of which had priority dates before November of 2002—that disclosed uses and properties of thalidomide and thalidomide analog compounds, including "Amino Thalidomide", *i.e.*, pomalidomide. Because patent prosecutions are *ex parte* and the PTO relies on the applicant to disclose all relevant information, acquiring the broad patent portfolio in the December 31, 2002 Exclusive Licensing Agreement reduced Celgene's risk that any of these patents would be asserted against them as prior art by a third party.

11. Fall of 2002: Celgene, along with Insogna and Zeldis, knew that pomalidomide and its use was in the public domain.

140. By the fall of 2002, scientists from multiple research centers had been studying and publishing findings regarding thalidomide analogs, including pomalidomide, for more than a decade. The specific attributes of pomalidomide were publicly disclosed, including:

- its anti-angiogenic properties,
- the fact and relative effectiveness in reducing TNFα levels,
- that pomalidomide inhibits angiogenesis,

[67] The terms of the December 31, 2002 licensing agreement (a three-way agreement between EntreMed, Children's, and Celgene) (the "December 31, 2002 Exclusive License Agreement") were disclosed in subsequent litigation filed by Children's against Celgene in 2013 arising out of a royalties dispute. *See Children's Medical Center Corp. v. Celgene,* 13-cv-11573 (D. Mass.), Complaint (ECF 1-1, filed July 2, 2013) at ¶ 6, describing the December 31, 2002 Exclusive License Agreement (ECF 85-4) at ¶¶ 4.1 and 4.3.

- that pomalidomide inhibits angiogenesis and multiple myeloma cell growth (whereas thalidomide only inhibits angiogenesis), and
- its use with dexamethasone.

141. By mid-2002, Celgene's own patents, and the portfolio it bought from Children's Hospital, had already disclosed the administration of pomalidomide to treat multiple myeloma.

142. By early fall of 2002, Celgene, along with Insogna and Zeldis, were aware of, and embroiled in, a dispute (which would lead to two lawsuits) with Boston Children's Hospital and Entremed over rights to the development and commercialization of lenalidomide and pomalidomide. Celgene, along with Insogna and Zeldis, knew that the D'Amato patent portfolio disclosed the uses of lenalidomide and pomalidomide to reduce TNFα levels and treat associated diseases such as multiple myeloma.

143. On December 9, 2002, Celgene obtained approval under an investigational new drug application (IND) to conduct tests using pomalidomide.

B. November 2002: Celgene began its fraudulent pursuit of method-of-use patents for pomalidomide.

144. On November 6, 2002, Celgene filed provisional patent application no. 60/424,600 generally claiming methods of using immunomodulatory compounds to treat various cancers, and specially claiming lenalidomide (identified by its chemical name, 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione, and by its then-used commercial name, Revlimid) and pomalidomide, (identified by its chemical name, 4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-1,3-dione, and by its then-commercial name, Actimid[68]) for treating refractory or relapsed multiple myeloma.[69] The application also reported the results of Phase I clinical trials for both compounds,

[68] Also referred to as CC-4047.

[69] "Refractory myeloma" means that the cancer is not responsive to or progresses within 60 days of the last line of therapy. "Relapsed myeloma" is previously treated myeloma that has progressed

trials that had been shaped by and based on the significant, reported scientific research over the prior two decades.

145. Starting from this November 6, 2002 application,[70] Celgene, along with Insogna and Zeldis, would seek a series of patents for methods of using lenalidomide and pomalidomide for the treatment of multiple myeloma. In doing so, they repeatedly misrepresented known material facts to, and omitted known material facts from, the U.S. patent office.

146. All of Celgene's method of treatment patents at issue here (the 8,198,262, 8,673,939, and 8,735,428) derive from the November 2002 provisional application. This means that all information publicly disclosed *before* November 6, 2002, including all of the patents, patent applications, and scientific articles described above, are prior art against which the novelty/inventiveness of these new method-of-treatment claims would be judged.

147. The family of applications and patents that issued in this family (and that were asserted in patent infringement litigation against Pomalyst ANDA filers) is illustrated by the following diagram of patent applications and issued patents.[71] The three relevant, fraudulently acquired, pomalidomide method of treatment patents are the '262, the '3939[72], and the '428.

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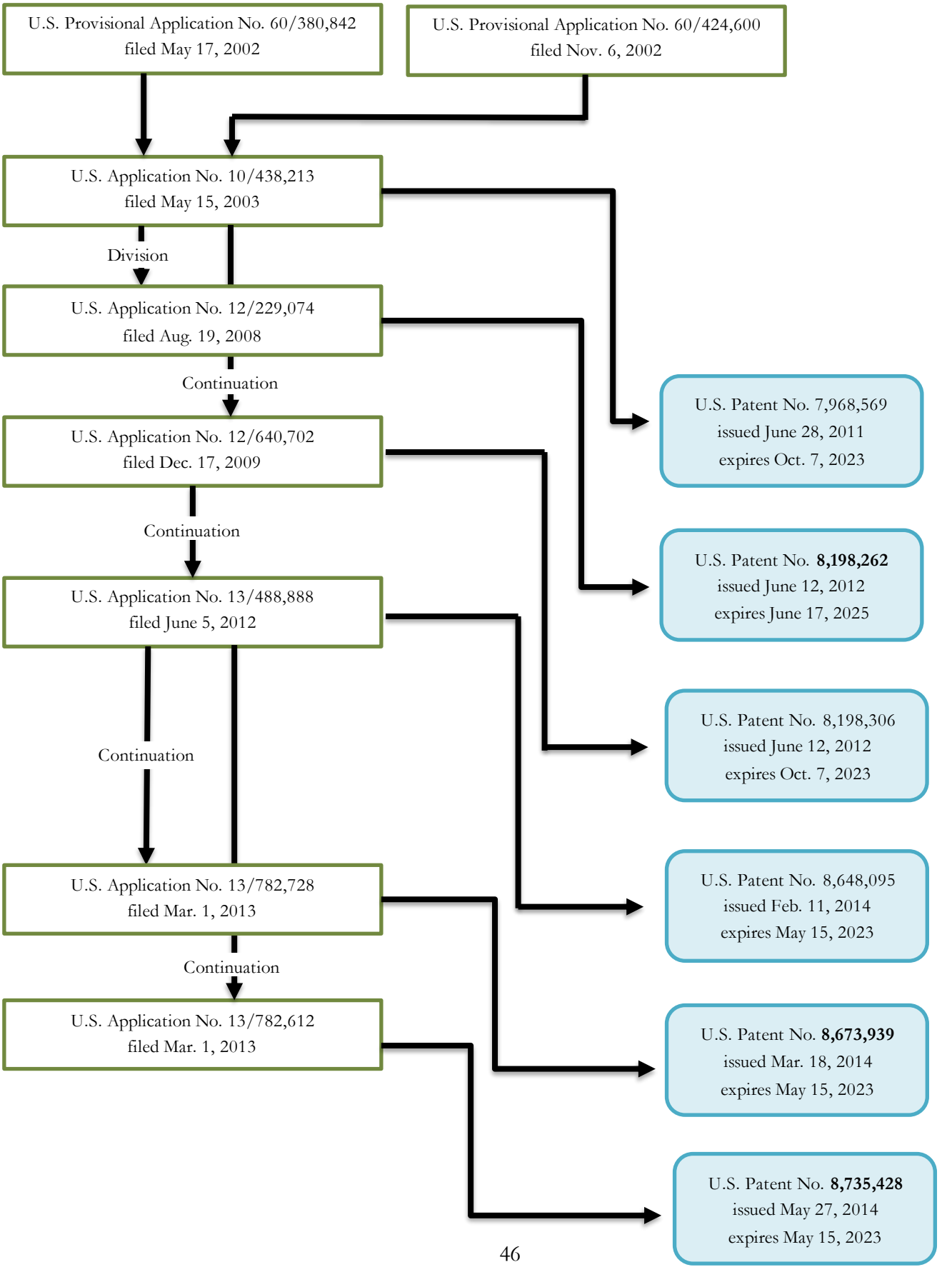
after previous therapy and needs new therapy. Parva Bhatt, Colin Kloock, & Raymond Comenzo, *Relapsed/Refractory Multiple Myeloma: A Review of Available Therapies and Clinical Scenarios Encountered in Myeloma Relapse*, 30 Current Oncology 2322, 2322 (2023).

[70] An earlier provisional application had been filed in May 2002 relating to treatments combining thalidomide analogs with large molecule proteins, and that application is sometimes attributed as being within this patent family. Presumably because that application related to treatments combining the analogs with the proteins, and not the analog alone, the November 6, 2002, application was treated as the relevant priority date by the parties during the subsequent patent litigation. We do the same here.

[71] "Expires" represents the patent expiration date exclusive of pediatric exclusivity ("PED"). The following patents have PEDs exclusivity: 8,198,262 (12/17/2023), 8,673,939 (11/15/2023), and 8,735,428 (11/15/2023).

[72] This patent is referred to as the '3939 (there is another Celgene patent ending in the same three digits: formulation patent 10,555,939, discussed *infra*). The formulation patent is referred to as the '5939.

THALIDOMIDE ANALOG METHOD-OF-USE PATENT TREE



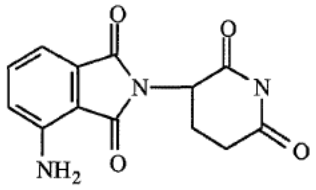
148. On May 15, 2003, Celgene filed patent application no. 10/438,213, which taught lenalidomide and its use for treating cancer, including multiple myeloma. This application would eventually result in the 7,968,569, which claimed a method of treating multiple myeloma through cyclical dosing of lenalidomide, *i.e.*, 21 consecutive days of administration followed by 7 days of rest, in combination with dexamethasone.

C. 2003: Celgene and Insogna dismantled D'Amato's patent portfolio disclosing pomalidomide.

149. While Celgene was building up its own pomalidomide patent portfolio, Celgene was also taking steps to bury the D'Amato pomalidomide patents and patent applications for which it had purchased licenses from Children's Hospital and Entremed.

150. Some of D'Amato's patents in the licensing agreement claimed the compound pomalidomide and its use in treating undesired angiogenesis, including U.S. Patent No. 7,153,867 (the '867) and U.S. Patent applications 09/899,344 (the '344 application), 09/966,895 (the '895 application), 10/166,539 (the '539 application), and 10/020,391 (the '391 application).

151. In the licensed patents and in his other published work, D'Amato routinely used the term "3-aminothalidomide" to refer to pomalidomide. For example, the '391 amended application claimed in claim 30: "A pharmaceutical composition compromising…3-amino thalidomide having the formula



…to reduce the effects of an angiogenesis-mediated disease." The compound depicted is pomalidomide.

152. Celgene licensed D'Amato's patents and pending patent applications, and Anthony Insogna took over as power of attorney for the '867 patent and '344, '895, '539, and '391 patent applications in March 2003.

153. Three months later, on October 14, 2003, Insogna sent a notice of abandonment for the '391 application. By the end of 2003, all four applications that claimed pomalidomide and methods of using pomalidomide had been abandoned. The '344 application was expressly abandoned on January 2, 2003, even though it was due to issue on January 14, 2003. The '539 application was expressly abandoned on February 11, 2003. The PTO mailed Insogna a notice of abandonment of the '895 application on September 17, 2003.

154. Insogna's conduct during these proceedings demonstrated that he knew that D'Amato used the atypical term "3 aminothalidomide" to refer to pomalidomide. For example, during his prosecution of D'Amato's '391 application, Insogna submitted a signed declaration stating that "3-aminothalidomide" was in fact pomalidomide.[73] Although Insogna was well aware of these facts, he would later conceal that "3-aminothalidomide," as used in a prior art reference written by D'Amato, referred to pomalidomide and indeed taught pomalidomide to treat multiple myeloma, the very invention for which Celgene was then seeking patent protection.

D. 2005-2006: FDA approved Celgene's blockbuster drugs Thalomid and Revlimid for treating multiple myeloma.

155. On December 27, 2005, the FDA approved lenalidomide, under the brand name Revlimid, for use in the treatment of patients with myelodysplastic syndromes,[74] a group of disorders

[73] Celgene Response to PTO after Non-Final Action, U.S. Patent Application 10/020,391, 13, 20 (July 11, 2003).

[74] It was specifically approved "for the treatment of patients with transfusion dependent anemia due to low or intermediate-1 risk myelodysplastic syndromes associated with a deletion 5 q cytogenetic abnormality with or without additional cytogenetic abnormalities." *See* Dec. 27, 2005 Final Approval Letter, available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2005/021880rev2.pdf (last accessed August 21, 2024).

that occur when blood-forming cells in bone marrow become abnormal (a condition considered a type of cancer).

156. On May 25, 2006, the FDA approved Celgene's new drug application for the use of thalidomide capsules, 50 mg, 100 mg, and 200 mg, under the brand name Thalomid, for the treatment of patients with newly diagnosed multiple myeloma. For treatment of multiple myeloma, the approved label stated that thalidomide is administered in combination with dexamethasone 40 mg.

157. On June 29, 2006, the FDA approved Celgene's NDA for lenalidomide 5 mg, 10 mg, 15 mg, and 25 mg capsules, under the brand name Revlimid, in combination with dexamethasone for the treatment of multiple myeloma patients who had received one prior therapy. The recommended starting dosage was 25 mg daily on days 1-21 of a 28-day repeated cycle with dexamethasone 40 mg. Lenalidomide 5 mg and 10 mg capsules had been approved approximately six months earlier for treatment of certain patient with transfusion-dependent anemia due to myelodysplastic syndromes.

E. 2008-2013: Celgene continued its fraudulent pursuit of method-of-use patents for pomalidomide.

1. August 2008: Celgene filed the application for the first of its pomalidomide method-of-use patents, which it obtained by fraud.

158. On August 19, 2008, Celgene, along with Insogna and Zeldis, filed patent application 12/229,074 claiming methods of treating multiple myeloma with pomalidomide (1 mg to 4 mg), with and without using dexamethasone and a cyclic dosing regimen. This application would eventually lead to the incorrect issuance of the 8,198,262 method of treatment patent.

159. The '262 patent applicant was inventor Zeldis. The attorney who prosecuted the application that led to the '262 patent was Insogna.

160. On June 24, 2010, the patent examiner issued an office action rejecting the claims based on obviousness and double patenting. For the obviousness rejection, the office relied on a combination of the '517, Davies (2001), and either the 6,555,554 or 6,281,230 to conclude that it would have been obvious to use the thalidomide analog pomalidomide (referred in the action as ACTIMID) in the cyclical treatment of multiple myeloma as it was a known effective agent in decreasing TNFα and that a skilled artisan would adjust dose depending on the level of disease and the potency of the drug. The double patenting objections also relied on the '517 and Davies to show that there would be double patenting over a series of five patents that already issued in Celgene's favor.

161. While the office action rejected the claims, it did so on a basis that required the *combined* teaching of the three specific references. The patent examiner was under the misimpression that neither the '517 nor Davies (2001) expressly taught pomalidomide, and that the '554/'230 did not expressly teach multiple myeloma. Nor did the patent examiner cite other earlier scientific literature or patents showing the treatment of multiple myeloma with pomalidomide itself. Rather, the examiner concluded—based only on the three references—that the references taken together showed the use of thalidomide and its analogs act directly on multiple myeloma cells, and that one of ordinary skill in the art would have been motivated by the reasonable expectation that the thalidomide analog pomalidomide (which is also effective in decreasing TNFα) would also be effective in the treatment of multiple myeloma since the decrease in TNFα provided the rationale for treating the disease with thalidomide.

162. On December 23, 2010, Insogna, on behalf of Celgene, submitted an amendment. In the amendment, Celgene, along with Insogna and Zeldis, made materially false and misleading statements intended to overcome the examiner's objections.

163. *Falsity regarding the '517 patent*. Celgene's response to the examiner's citation to the '517 was false and misleading. In the office action, the examiner had mistakenly attributed to the '517 specific statements of the treatment of multiple myeloma with thalidomide and dexamethasone. As he would make clear later, the reference should have been to Kyle (2001). And in describing the '517, the examiner twice mentioned that the '517 "did not expressly teach ACTIMID [pomalidomide]." But this was incorrect. In fact, the '517 claims a method of reducing undesirable levels of TNFα where the compound is pomalidomide, which the '517 discloses is "a valuable therapeutic strategy for the treatment of. . . . cancer. . . ." The '517 specifically disclosed pomalidomide and its use to reduce TNFα.

164. But in its response, Celgene simply noted that the '517 did not have the material in it that the examiner had mistakenly reported. Instead, Celgene hid from the examiner the more significant error in the analysis: the dispositive fact that the '517 patent expressly taught pomalidomide.

165. Celgene owns the '517 patent, the compound patent for Celgene's multi-billion dollar-a-year drug Revlimid. The '262 patent applicant, Zeldis, and his attorney, Insogna, both knew the '517 patent specifically disclosed pomalidomide, and they knew that the '517 claimed a method of using pomalidomide to reduce TNFα and taught that reduction of TNFα was a means of treating cancer. They also knew of the potential for confusion on the part of the patent examiner on the subject (given different ways to refer to pomalidomide). Yet Celgene (along with Insogna and Zeldis) fraudulently withheld and omitted the true import of the '517 patent on patentability, and did so in order to obtain the '262 patent.

166. Insogna knew that the '517 taught pomalidomide. By this time, Insogna had been representing Celgene for years and was intimately knowledgeable on all aspects of Celgene's thalidomide analog portfolio. He directly worked on the '517 patent prosecution itself. At the time,

the '517 patent was (and would continue to be) the cornerstone of Celgene's Revlimid empire, raking in profits of nearly $2.5 billion on the drug in 2010. Yet Insogna nonetheless reiterated and implicitly reaffirmed the patent examiner's mistaken belief that the '517 did not teach pomalidomide.

167. Zeldis also knew that the '517 taught pomalidomide. Zeldis had been an executive at Celgene since 1997, specifically serving as Chief Medical Officer since 1999. As a senior executive, scientist, and inventor at Celgene, Zeldis understood what the '517, Celgene's most important patent, claimed, including teaching pomalidomide.

168. The only logical inference from the fact that Celgene did, in fact, choose to comment on the contents of the '517 and yet chose not to comment on the known aspects of the '517 that render claims of the '262 patent unpatentable is that Celgene (along with Insogna and Zeldis) made that statement in support of patentability with the intention that the examiner rely on it and issue the patent.

169. Celgene, along with Insogna and Zeldis, exploited the examiner's incorrect belief that the '517 did not teach pomalidomide by repeating it and failing to correct it, thus reinforcing the examiner's incorrect understanding. Celgene wrote: "The PTO admits that the primary reference [the '517] does not teach ACTIMID (page 5 of the Action). Thus, the primary reference does not direct the skilled person to use the recited compound in the treatment of multiple myeloma." This is incorrect. Celgene (along with Insogna and Zeldis) knew that the '517 patent *did* teach pomalidomide.

170. *Falsity regarding Davies (2001)*. Celgene (along with Insogna and Zeldis) also repeated and perpetuated the examiner's mistaken belief that Davies did not teach pomalidomide. Davies (2001) disclosed that thalidomide and the 3 immunomodulatory drugs studied (referred to as ImiD1, ImiD2, and ImiD3) can act directly on multiple myeloma cells and are useful in relapsed/refractory disease. Celgene coined the term "immunomodulatory drugs" or "IMiDs" to refer to its thalidomide

analogue drugs, most prominently pomalidomide and lenalidomide. Davies (2001) did not identify the three IMiDs by chemical structure or by chemical name, a fact that Celgene capitalized on to mislead the examiner into believing that pomalidomide was not one of the drugs studied in Davies (2001). This was false. Pomalidomide has been one of Celgene's two most important IMiDs since its research into thalidomide analogues began (the other being lenalidomide). Davies' teachings are about pomalidomide. Celgene parrots the examiner's incorrect belief ("the Office admits that [Davies] does not teach ACTIMID."). Celgene's agents Insogna and Zeldis knew this was false, as two of Celgene's senior scientists, George Muller and David Stirling, were involved in the Davies study and are named authors on it.

171. *Falsity regarding D'Amato (2001).* Celgene (along with Insogna and Zeldis) also concealed that D'Amato (2001) taught pomalidomide for the treatment of multiple myeloma.

172. During the prosecution that led to the '262 patent, the patent examiner focused on whether the prior art taught pomalidomide or taught treating multiple myeloma. The patent examiner makes no mention of D'Amato (2001) during the patent prosecution, even though D'Amato (2001) teaches not just one, but both, of these critical points, *i.e.*, the use of pomalidomide to treat multiple myeloma. This fact appears to have been lost on the examiner, perhaps due to confusion regarding nomenclature for pomalidomide.

173. But Celgene, along with Insogna and Zeldis, knew better. In response to the examiner's initial rejection, they engaged in a misdirection, arguing that two other patents, the '230 and '554, did not teach the use of pomalidomide to treat cancer. But in making these arguments, Insogna and Zeldis concealed that D'Amato 2001 *did* specifically teach the use of pomalidomide to treat multiple myeloma.

174. Celgene, along with Insogna and Zeldis, knew this material information, but fraudulently omitted the truth about D'Amato (2001) to the examiner. While both the '262 patent

application and D'Amato (2001) include diagrams showing the same compound, pomalidomide, the import of the D'Amato (2001) reference was not apparent. Zeldis and Insogna were knowledgeable about Dr. D'Amato's research involving thalidomide compounds, including pomalidomide, and knew D'Amato (2001) taught pomalidomide to treat multiple myeloma.

175. Zeldis knew D'Amato (2001) taught pomalidomide. Zeldis was actively studying and pursuing patents for pomalidomide for the treatment of multiple myeloma and therefore would have been familiar with studies involving the same compound to treat the same disease. Zeldis was also an executive at Celgene during the '517 reexamination, the lawsuits with EntreMed, and Celgene's December 30, 2002 Exclusive License Agreement to acquire D'Amato's patents, and D'Amato's research was the focus of all these proceedings. Given his role as a clinical researcher and senior executive at Celgene, Zeldis was familiar with D'Amato's research and with D'Amato's practice of using "3 aminothalidomide" to refer to pomalidomide. Zeldis knew that D'Amato (2001) taught pomalidomide to treat multiple myeloma, yet failed to disclose this material fact during the prosecution of the '262 patent so that he and his employer Celgene could obtain the patent.

176. Insogna knew that D'Amato (2001) used 3-aminothalidomide to refer to pomalidomide. Pursuant to the December 30, 2002 Exclusive License Agreement, Celgene had licensed more than 75 patents and patent applications on which D'Amato was an inventor or co-inventor.[75] In six of these patents and patent applications, D'Amato repeatedly used "3 aminothalidomide" to refer to pomalidomide, including by labeling diagrams of pomalidomide as "3 aminothalidomide."[76] Insogna was designated to receive notice under this licensing agreement.[77]

[75] December 31, 2002 Exclusive License Agreement at ¶ 7.1(d) and Appendix A.

[76] *See e.g.*, U.S. Patent Applications 10/020,391 and 09/966,895.

[77] *Id.* at ¶ 11.1.

177. Following the December 31, 2002 Exclusive License Agreement, Insogna took over the prosecution and management of the D'Amato patent and patent application portfolio.[78] In this role, Insogna knew that D'Amato used "3 aminothalidomide" to refer to pomalidomide. For example, during the prosecution of the '391 D'Amato patent application, Insogna filed revised claim language stating that the compound D'Amato referred to as "3-aminothalidomide" was "4-(amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline- 1,3-dione," the name Celgene and Insogna regularly used to refer to pomalidomide, demonstrating Insogna was well aware D'Amato used "3 aminothalidomide" to refer to pomalidomide.

178. In short, during the prosecution of the '262 patent, including in the December 23, 2010 amendment and response, Celgene, along with Insogna and Zeldis, deceived the examiner into withdrawing prior rejections by misleading the examiner and concealing from him a wealth of prior art of which they were aware and which they knew would render the application not allowable.

179. The ruse worked. On August 9, 2011, the patent examiner, relying upon the misrepresentations by Celgene (with Insogna and Zeldis), withdrew the prior rejections, including his objections based on the '517. In the office action, the examiner made no further mention of the '517 as an objection to obviousness, nor as a basis to reject the claims for double patenting with the five patents in the '517 patent tree.

180. Instead, in the August 2011 office action, the examiner again rejected all claims, this time relying on Kyle (2001) (the correct reference for the material regarding cyclical dosing of

[78] Given his role in prosecuting D'Amato's '391 patent application, among other patents, for Celgene, generic company Hetero subsequently sought to depose Insogna in Celgene's patent infringement litigation against Hetero. In opposing Insogna's motion to quash the subpoena, Hetero explained that Insogna's prosecution of D'Amato's patents involved "expressly abandon[ing] them, even after one had received a notice of allowance from the patent office." Hetero's Opposition to Mot. To Quash at 11, *In re Subpoena on Third Parties Anthony Insogna and David Gay*, No. 3:19-cv-01589-LAB-AHG (S.D. Cal. Oct. 17, 2019), ECF 9.

thalidomide analogs with dexamethasone previously attributed to the '517) and several other references (Davies (2001), Corral (1999), Muller (1999), and the '554/'230). The examiner wrote it "would have been obvious to one having ordinary skill in the art at the time the invention was made to treat [multiple myeloma] with pomalidomide as suggested by Kyle[,] Davies, Corral and Muller by administering pomalidomide in a tablet or capsule . . . ."

181. On December 20, 2011, Celgene, again along with Insogna and Zeldis, filed an amendment and response that, made at least three further false statements and material omissions with the intent of overcoming the examiner's objections.

182. *Falsity regarding treatment of multiple myeloma with pomalidomide.* Celgene (along with Insogna and Zeldis), misrepresented that the treatment of multiple myeloma with pomalidomide had not been publicly disclosed previously.[79] That was knowingly false. The prior art, including D'Amato (2001), Lentzsch (2001), Lentzsch (2002), Schey (April 2002), and Schey (October 2002), specifically taught pomalidomide for the treatment of multiple myeloma and/or relapsed/refractory multiple myeloma. Indeed, this teaching was fully encompassed within the D'Amato (2001) prior art reference.

183. *Falsity regarding relative power*. Celgene (along with Insogna and Zeldis), made misleading statements and material omissions suggesting that the use of one thalidomide compound over another had not been publicly disclosed previously. That was knowingly false. The relative power of pomalidomide to reduce TNFα levels was previously publicly disclosed. For example, as part of the 1998-1999 reexamination of the '517 Revlimid patent, Celgene submitted data to the patent office showing that pomalidomide was purportedly 10,000-fold more active than the comparator compound selected by Celgene.

[79] *See* December 20, 2011 amendment and response at 6 ("there is no suggestion in the cited art that pomalidomide is effective to treat multiple myeloma.").

184. *Falsity regarding treatment for refractory patients*. Celgene (along with Insogna and Zeldis) misrepresented that pomalidomide (combined with dexamethasone) produced unexpected results for treating relapsed or refractory multiple myeloma patients. That was knowingly false, as there was nothing surprising about the fact that the more potent thalidomide analog, pomalidomide, would be used where the multiple myeloma patient had become relapsed or refractory to less potent analogs such as thalidomide and lenalidomide.

185. In short, the December 20, 2011, amendment and response was intended to deceive the examiner into withdrawing prior rejections, having the examiner not appreciate the full prior public disclosures regarding the potential to treat multiple myeloma using pomalidomide, and to believe the ostensible unexpected results were a lawful basis to allow the claims.

186. On March 1, 2012, Celgene (along with Insogna's associate) initiated a call with the patent examiner (and another) to discuss the patent application. Celgene's ruse worked once again. As the examiner summarized the interview:

> "Discussed potential allowability of claims if independent claims are amended to incorporate the limitations of claim 1 of U.S. Pat 7,968,569. Particularly the cyclical administration of the current amounts of the compound for 21 consecutive days followed by 7 consecutive days of rest from administration of the compound in a 28 day cycle in combination with 40 mg of dexamethasone."[80]

187. The concept of cyclical administration of pomalidomide in combination with dexamethasone was not novel. For example, Kyle (2001) discloses methods of treating multiple myeloma by cyclically administering thalidomide and dexamethasone. Coleman (2002) taught the specific amount of 40 mg of dexamethasone combined with thalidomide to treat multiple myeloma. And Cohen (1982) taught the specific 28-day dosing regimen, *i.e.*, 21 days administration of an anticancer drug followed by 7 days of rest, in combination with dexamethasone. In treating cancer, it

[80] Typographical errors and misspellings corrected.

has long been a routine practice to administer the drug for a set period of time followed by a rest period. As the National Cancer Institute explains: "Some targeted therapies are given in cycles. A cycle is a period of treatment followed by a period of rest. The rest period gives your body a chance to recover and build new healthy cells."[81] The cyclical treatment of cancer is well known; and there is nothing novel about a week-based cycle (*i.e.*, 21 days of treatment followed by 7 days of rest), which one would expect because it is predictable and easy to adhere to.

188. On March 15, 2012, Celgene (along with Insogna and Zeldis) submitted a response and statement of interview summary. The response amended the claims as contemplated at the March 1, 2012, meeting and reiterated that the examiner should withdraw all obviousness objections based on the representations it had made in its December 20, 2011, response.

189. On April 9, 2012, the patent examiner issued a notice of allowance of the '262 application. Celgene had obtained the '262 patent by fraud.

190. The examiner would not have allowed the '262 patent to issue absent the fraud committed by Celgene, Insogna and Zeldis.

191. In addition to the above fraud, the '262 patent is also manifestly invalid as obvious over the prior art. To highlight just a few references: Celgene's own patent, the '517, claimed a method of using pomalidomide to reduce TFNα and taught reduction of TNFα as a cancer treatment; Davies (2001) taught IMiDs, including pomalidomide, to treat multiple myeloma and relapsed/refractory disease; D'Amato (2001) taught the use of pomalidomide specifically to treat multiple myeloma; Kyle (2001) taught treatment of multiple myeloma by administering thalidomide

[81] *Targeted Therapy to Treat Cancer*, National Cancer Institute https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies (last updated May 31, 2022).

in combination with dexamethasone;[82] Hideshima (2000) taught thalidomide and its analogues' ability to overcome drug resistance of multiple myeloma cells; Lentzsch (2001), Lentzsch (2002), Schey (April 2002), and Schey (October 2002) taught pomalidomide to treat multiple myeloma and/or relapsed/refractory multiple myeloma; Coleman (2002) taught 40 mg of dexamethasone combined with thalidomide to treat multiple myeloma; and Cohen (1982) taught the 21 day administration of an anticancer drug, followed by 7 days of rest, in combination with dexamethasone. The '262 did not claim anything beyond what was already known in the prior art.

192. In short, the '262 (and Celgene's other Pomalyst method of treatment patents) were invalid from their inception, as well as unenforceable due to Celgene's fraud on the patent examiner.

2. Shortly after the patent examiner allowed the '262, Celgene submitted its new drug application for Pomalyst.

193. On April 10, 2012, Celgene submitted a new drug application (NDA) to the FDA for approval to market Pomalyst (pomalidomide) capsules.

194. On February 8, 2013, the FDA approved Celgene's NDA for pomalidomide 1 mg, 2 mg, 3 mg and 4 mg capsules, under the brand name Pomalyst, in the treatment of patients with multiple myeloma who had received prior lenalidomide therapies and demonstrated disease progression. The recommended dosage was 4 mg daily on days 1-21 of a repeated 28-day cycle which could be taken with dexamethasone.

195. Following FDA approval, Celgene was granted a period of regulatory exclusivity. For new chemical entities, such as Pomalyst, the brand is granted a five-year exclusivity period. This

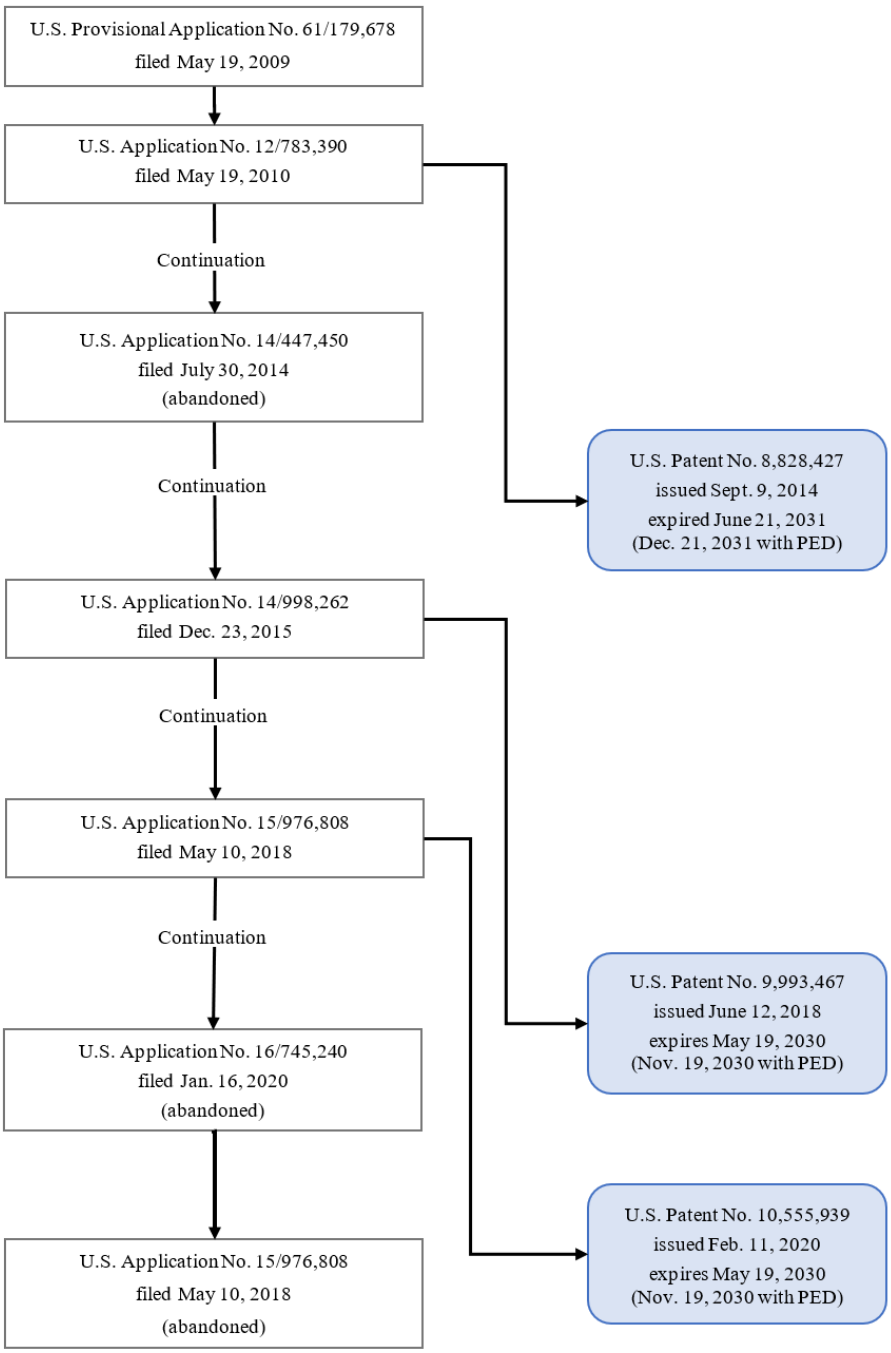
[82] Kyle, Robert A., and S. Vincent Rajkumar. *Therapeutic Application of Thalidomide in Multiple Myeloma.* Seminars in Oncology 28, no. 6 583–87 (Dec. 1, 2001) doi:10.1016/S0093- 7754(01)90028- 4, summary available at https://journals.scholarsportal.info/details/00937754/v28i0006/583_taotimm.xml (last accessed August 21, 2024).

would provide a period for NCE exclusivity to February 8, 2018. Celgene would later tack onto this, by reason of its ill-gotten Pomalyst patents, further periods of exclusivity.

F. In 2009, Celgene also began seeking a series of formulation patents for Pomalyst by falsely claiming "unexpected results."

196. Beginning in 2009 (and continuing for over a decade), Celgene also sought a series of formulation patents for pomalidomide, falsely claiming its formulation showed "unexpected results" that were "surprising." Below is the Pomalyst formulation patent family:

POMALYST FORMULATION PATENT TREE



1. The prior art had already disclosed pomalidomide formulations as well as the need to address pomalidomide's instability issues.

197. Prior to Celgene's formulation patent applications, it was well known and well documented in the scientific community that thalidomide compounds are notoriously unstable due to hydrolysis (*i.e.*, degradation of the compound in the presence of water).[83]

198. There are also numerous sources, including Remington's Pharmaceutical Sciences, a pharmaceutical textbook first published more than 100 years ago, that teach methods of preparing oral dosage forms of various pharmaceutical compositions. As relevant here, Remington's teaches: (1) the range of capsule sizes that can be swallowed and the capacity of each capsule size to hold a specified amount of powdered drug material; (2) the use of excipients, such as mannitol; (3) the advantages of spray drying mannitol; and (4) the amount of filler or binder typically used.[84] In addition, sodium stearyl fumarate has been known since at least the 1990s to be an acceptable lubricant for capsules.[85]

199. Additionally, Schey (April 2002) taught pomalidomide at specific dosing amounts, up to a maximum tolerated dosing amount of 5 mg per day.

200. On December 21, 2006, Celgene filed patent application no. 11/645,319 claiming pomalidomide in combination with an acceptable carrier or excipient. Zeldis was the first named inventor on the '319 application, and Insogna filed the application on behalf of Celgene. The '319 patent application disclosed that pregelatinized starch and mannitol are acceptable excipients for use

[83] *See, e.g.*, H. Schumacher, R. L. Smith, and R.T. Williams, *The Metabolism of Thalidomide: The Spontaneous Hydrolysis of Thalidomide in Solutions,* Brit. J. Pharmacol. (1965), 25, 324–337 ("in this paper we shall describe the conditions for the spontaneous hydrolysis of thalidomide in aqueous solution at various *p*H values.") available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1510736/pdf/bripharmchem00017-0044.pdf (last accessed August 21, 2024).

[84] The specific edition cited by the PTO is the 17th edition of Remington's Pharmaceutical Sciences (published in 1985) ("Remington's").

[85] *See, e.g.*, the 5,593,696 patent ("McNally").

in combination with pomalidomide. The '319 patent application was rejected four times, including for obviousness and double patenting. It was subsequently abandoned.

201. On May 19, 2009, Celgene filed provisional patent application no. 61/179,678. Insogna filed the '678 provisional application on behalf of Celgene. All the formulation patents at issue (the 8,828,427, 9,993,467, and 10,555,939) are related to this provisional patent application and therefore have a priority date of May 19, 2009. By this date, the '319 patent application, Remington textbook, and McNally's '696 patent, had all been disclosed in the prior art, and it was well known that thalidomide and its analogs faced stability issues due to hydrolysis.

2. Celgene defrauded the patent office to obtain the '427 formulation patent.

202. On May 19, 2010, Celgene's Senior Director of Pharmaceutical Technology and Development, Anthony Tutino, filed patent application no. 12/783,390, which would lead to the '427 patent, the first of the Pomalyst formulation patents here at issue. Insogna prosecuted the '390 application on behalf of Celgene and its agent Tutino. The proposed patent claimed an oral dosage form of a given weight (*e.g.*, weighing "about 62.5 mg") comprised of pomalidomide and a pharmaceutically acceptable carrier or excipient, such as mannitol, pregelatinized starch, and sodium stearyl fumarate.

203. On April 24, 2012, the examiner rejected the patent application as obvious in light of the prior art, stating: "It would have been *prima facie* obvious to a person of ordinary skill in the art at the time of the invention to have made oral dosage forms comprising pomalidomide and excipients such as mannitol and pre-gelatinized starch, with a reasonable expectation of success because Zeldis et al. taught such oral dosage forms." The examiner also pointed to Remington's as teaching capsule sizes and the benefits of spray drying common diluents like mannitol and to McNally as showing sodium stearyl fumarate is a known lubricant in the art.

204. The examiner also noted that, as defined and used in the patent application, since Celgene used the term "about" to describe the claimed amounts of pomalidomide and excipients, the amounts would be ranges: "The claims contain the term 'about' in front of quantities of active agents and excipients. Based on the specification the term 'about' is defined as a dose, amount, or weight percent within 30%, 25%, 20%, 15%, 10%, or 5% of the specified dose, amount, or weight percent. . . . Therefore, the claimed amounts of active and excipients are viewed as ranges." In other words, Celgene sought to define the scope of the claims very broadly.

205. On August 16, 2012, Celgene's counsel Insogna submitted an amendment and response arguing, "although Zeldis may generally disclose a laundry list of compostions [sic] containing pomalidomide in combination with a broad range of possible excipients that may be used in such compositions, there is no disclosure in Zeldis that would have prompted one skilled in the art to prepare a composition having pomalidomide at the specified amounts, along with the particular binders and fillers" as claimed. Celgene and Insogna concealed that the prior art, including Schey (April 2002), disclosed pomalidomide dosage amounts up to a maximum tolerated dosage of 5 mg per day. Celgene dismissed Remington and McNally as prior art on the basis that they did not teach the advantages of the specific oral dosage forms claimed.

206. On November 15, 2012, (and despite Celgene's misrepresentations and omissions), the examiner again rejected the patent application on the basis that the claimed invention was obvious over Zeldis in view of Remington's and McNally's. The patent examiner also rejected the claims for failure to comply with the written description requirement, stating that Celgene failed to "convey to one skilled in the relevant art that the inventor . . . at the time the application was filed, had possession of the claimed invention," and for indefiniteness.

207. The examiner was also not persuaded by Celgene's claims regarding "unexpected results" in part because the submission "lack[s] data that shows alleged unexpected results." The

patent examiner continued, "[i]n the instant case the applicant did not show that the results were unexpected, unobvious, and of both statistical and practical significance. Applicant instead provided a conclusion that advantageous and unexpected properties were observed without showing any evidence that supports those conclusions . . . this is not sufficient to overcome obviousness."

208. On June 17, 2013, to overcome the examiner's repeated rejections of the patent application, Celgene, along with Insogna and Tutino, submitted false data ostensibly in support of Celgene's assertion of patentability based on "unexpected results." The Tutino Declaration does not specify when the reported testing was conducted, vaguely stating that "tests have been conducted between pomalidomide and various candidate excipients." Based on these undated tests, Mr. Tutino asserted that the claimed invention is patentable because it was "unexpected" that many of the other pomalidomide/excipient combinations he tested posed stability issues over time. The assertion was unfounded.

209. Thalidomide is notoriously unstable due to hydrolysis (*i.e.*, degradation of the compound in the presence of water), a fact that has been well known and documented in the scientific community for decades. Tutino feigned ignorance of these known stability issues and, when he encountered hydrolysis (which he addressed through standard, routine optimization), proclaimed this was "unexpected." There would have been nothing surprising or "unexpected" about these stability issues given the known tendency of thalidomide compounds to degrade in the presence of water. And it would have been routine practice to address these known stability issues as part of the formulation process. Insogna and Tutino deceived the patent examiner when they told the examiner otherwise.

210. Following Celgene's submission of the misleading Tutino Declaration, the examiner allowed the '427 formulation patent to issue.

211. The '427 would not have issued but for the false representations and deliberate omissions in the declaration regarding the prior art and the purportedly unexpected results. This was material information on which the patent examiner justifiably relied; although the examiner had repeatedly rejected the patent as obvious, following the submission of the Tutino Declaration, the patent was allowed to issue.

212. Although the examiner allowed the '427 patent to issue, it allowed only a narrow set of claims (claims that were easy to design around to avoid infringement). The approved claims are for a capsule comprising pomalidomide, pregelatinized starch, sodium stearyl fumarate, and spray-dried mannitol, where the capsule is one of six specific weights, *i.e.*, "[a]n oral dosage form in the form of a capsule which weighs [x] mg. . . ." where "[x]" is either 62.5, 125, 250, 180, 240, or 300 mg. A generic manufacturer would readily be able to design around this patent by, *inter alia*, developing a capsule with a weight other than one of the six weights claimed by the patent.

213. The '427 was invalid due to Celgene's fraud on the patent office, and additionally it was so narrow that a generic manufacturer could easily design around it. Therefore, the '427 should not have been a barrier to generic entry.

G. Celgene defrauded the patent office to obtain two more method of treatment patents (the '428 and '3939).

214. On March 1, 2013, Celgene filed two patent applications seeking to extend or broaden method-of-use patent protection for pomalidomide. The applications (nos. 13/782,612 and 13/782,728) continued in the '262 family and claimed priority back to the November 2002 provisional application. Zeldis is the first named inventor on both applications, which would lead to the '428 and the '3939 method of treatment patents, respectively.

215. Patent application no. 13/782,612 (leading to the '428) claimed *inter alia* a method of treating multiple myeloma with pomalidomide for 21 days followed by 7 consecutive days of rest, where the multiple myeloma is relapsed and/or refractory and there is demonstrated disease

progression after certain specified treatments. Although the proposed claims included a dependent claim for the administration of pomalidomide in combination with dexamethasone, the independent claim did not specify treatment in combination with dexamethasone.

216. The independent claims of the '3939 patent are the same as the '428, except the '3939 states that the compound is to be administered in "one or more cycles, each of which comprises administering the compound for a period of time followed by a period of rest," rather than specifying the exact cyclical schedule (*i.e.*, 21 days followed by 7 consecutive days of rest). The two patents were prosecuted in parallel, with essentially the same submissions, meetings, and evidence; the following discussion summarizes the prosecution history for the '428, which is substantially similar for the '3939.

217. On June 11, 2013, the examiner interviewed Celgene regarding the method of treatment patent application. On July 9, 2013, the examiner rejected the claims on the basis of double patenting over the '262.[86] The patent examiner also rejected the claims because "the claimed invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made." The prior art references cited by the examiner included Kyle (2001), Davies (2001), Corral (1999), Muller (1999), and the '554. Regarding the claims "wherein the previous therapy is, *inter alia,* thalidomide, lenalidomide or a proteasome inhibitor," the examiner stated in part, "one of ordinary skill in the art would have understood that [pomalidomide] would provide benefits in treating [multiple myeloma ("MM")] whether the patient had previous therapy with thalidomide, lenalidomide, proteasome inhibitor, etc. The skilled artisan would have at least found it obvious to try in these patients as well as others with MM."

[86] Although the non-final rejection refers to U.S. Patent No. "8,198,232", it is clear from context that the Examiner is speaking of Celgene's U.S. Patent No. 8,198,262, including that Celgene files a terminal disclaimer over the '262 patent and the '232 patent is unrelated and never mentioned again.

218. On October 4, 2013, the patent examiner interviewed Celgene representatives, including Celgene's attorney Ms. Moon; Dr. Anjan Thakurta, Senior Director in Translational Development at Celgene; Robertson-Chow for "Celgene Corporation, Assignee of the present application"; and Wei Zhang, the attorney for the patent applicant, Zeldis. According to the interview summary,[87] in order to overcome the examiner's rejection of the patent, the "Applicant submitted that the claims, as is, are patentable because pomalidomide (POM) alone was shown to unexpectedly treat multiple myeloma that is or has become resistant to lenalidomide (LEN). . . . Applicant submitted that one of ordinary skill in the art would not have recognized this because, inter alia, the compounds are so close in structure." The examiner suggested that Celgene submit the argument and supporting data as a declaration.

219. On October 8 and 9, 2013, to address the examiner's double patenting objection, Celgene filed the following terminal disclaimers:

Patent application	Resulting patent	Terminal disclaimer as to:
13/782,612	'428	(a) the '262
13/782,728	'3939	(a) the '262 and (b) any patent resulting from patent application no. 13/782,612

220. On October 9, 2013, to address the examiner's request for a sworn statement of Celgene's assertions made during the examiner interview, Celgene submitted the declaration of Thakurta (the "Thakurta Declaration") along with an Amendment and Request for Reconsideration. Thakurta was not a clinician and, at the time he produced this opinion, had no experience working on clinical trials. Nor was Thakurta a registered physician involved in treating patients. Thakurta does not appear to be a person qualified to offer an opinion (a "person of ordinary skill in the art" or "POSA") on the matters set forth in his declaration. In addition, the Thakurta Declaration makes

[87] The interview summary is dated October 13, 2013.

fraudulent misrepresentations and omissions of material facts regarding "unexpected results," and does not support a finding of patentability.

221. Thakurta's claims regarding unexpected results proceed from two premises. First, he states that three studies, Jagannath (2013),[88] Siegel (2013),[89] and Richardson (2011),[90] show that patients with relapsed or refractory multiple myeloma previously treated with lenalidomide had a clinically significant response rate when treated with pomalidomide. Second, Thakurta states (without citation or reference to any timeframe) that it "has been surprisingly found that resistance of multiple myeloma cells to pomalidomide and lenalidomide is not reciprocal," *i.e.*, if a patient is first treated with pomalidomide and develops a resistance to it, lenalidomide will not work. From these two premises, Thakurta concludes: "It is therefore my opinion that the results of the studies for treating relapsed and/or refractory multiple myeloma with single-agent pomalidomide would have been unexpected and surprising at the time the claimed invention was made." The Thakurta Declaration suffers from misrepresentations of fact and defects of logic.

222. Thakurta deceptively omits that, at the time of the claimed invention, the use of thalidomide analogues for the treatment of relapsed/refractory disease and the ability of thalidomide analogues, including pomalidomide, to overcome drug resistance of multiple myeloma cells was well

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[88] Sundar Jagannath, Craig C. Hofmeister, Rachid C. Baz, David Samuel DiCapua Siegel, Ravi Vij, Christine Chen, Sagar Lonial, Kenneth Carl Anderson, Min Chen, Mohamed H. Zaki, and Paul Gerard Guy Richardson, *Pomalidomide (POM) with or without low-dose dexamethasone (LoDEX) in patients (Pts) with relapsed and refractory multiple myeloma (RRMM): MM-002 phase II age subgroup analysis,* Journal of Clinical Oncology 2013 31:15 (suppl. Abstr. 8532), available at https://ascopubs.org/doi/abs/10.1200/jco.2013.31.15_suppl.8532 (last accessed August 21, 2024).

[89] Siegel, D. et al, *Long-term safety and efficacy of pomalidomide (POM) with or without low-dose dexamethasone (LoDEX) in relapsed and refractory multiple myeloma (RRMM) patients enrolled in the MM-002 phase II trial*, J Clin Oncol 31, 2013 (suppl; abstr 8588), available at https://ascopubs.org/doi/abs/10.1200/jco.2013.31.15_suppl.8588 (last accessed August 21, 2024).

[90] Richardson et al., *13th International Myeloma Workshop Abstract Book*, Haematologica 2011; 96 (Suppl. 1):O-12, available at https://haematologica.org/article/download/5980/29772 (last accessed August 21, 2024).

known in the prior art.[91] It was also known that pomalidomide was many times more potent than other thalidomide analogs, including lenalidomide. Celgene had already, as part of the 1998-1999 reexamination of the '517, touted the ostensible 10,000-fold increase in activity represented by pomalidomide (which in fact was 3-4 times). It was false to assert that pomalidomide's efficacy was surprising. There would have been nothing surprising about the fact that, once a patient's myeloma had become resistant to one thalidomide analog, the patient would be moved to a more potent thalidomide analog. Nor would it have been surprising that, if a patient's myeloma became resistant to the analog with greater potency, a less potent analog would not be effective. Thakurta's assertions to the contrary were false and intended to defraud the examiner into allowing the patent.

223. Thakurta made these deceptive representations and omissions with the intent to deceive the patent examiner. The examiner justifiably relied on the information provided by Thakurta, as evidenced by the examiner's reversal of its prior decisions rejecting the patents, allowing the patents to issue after Thakurta submitted his declaration.

224. In addition to Thakurta's fraudulent declaration, during the '428 and '3939 patent prosecutions, Celgene reiterated many of the same fraudulent misrepresentations and omissions it made to obtain the earlier method of treatment patent, the '262. For example, in an October 9, 2013 response, Celgene (again) repeated and perpetuated the examiner's mistaken belief that Davies (2001) did not teach pomalidomide, when in fact it taught pomalidomide to treat multiple myeloma and relapsed/refractory disease. Celgene also failed to disclose the truth about the '517 and D'Amato (2001).

225. As the first named inventor of both the '428 and the '3939 and prominent clinical researcher and senior executive at Celgene, Zeldis knew the truth, but stood by as Thakurta made

[91] *See, e.g.*, Hideshima (2000), Webber (2000), Dimopoulous (2001), Davies (2001), Schey (April 2002), and Schey (October 2002).

these false and misleading statements and material omissions during the course of the '428 and '3939 patent prosecutions in violation of his duty of candor and good faith to the examiner.

226. Through the deception of its agents, including Zeldis and Thakurta, Celgene achieved its goal. On March 18, 2014, and May 27, 2014, respectively, the examiner issued the '3939 and '428 patents, further extending Celgene's unlawful Pomalyst monopoly. Absent its deceptive representations and deliberate omissions, neither the '428 nor the '3939 would have issued. Both patents are unenforceable due to the fraudulent conduct of Celgene and its agents, and invalid as obvious over the prior art.

H. Celgene fraudulently procured a second Pomalyst formulation patent (the '467).

227. On December 23, 2015, Celgene filed patent application 14/998,262, which would lead to the '467 formulation patent. The named inventor on the patent application was Tutino.

228. As originally styled, the application sought to expand the scope of the previous formulation claims (which required formulations in absolute weight terms) by now claiming formulations in terms of the relative weight of pomalidomide to the combined binders and fillers.

229. Over the next two and a half years, the patent examiner repeatedly, and correctly, rejected the claims in the application as obvious.

230. On February 7, 2017, the examiner rejected the claims for a third time, stating in part:

> Applicant's arguments directed to picking and choosing and impermissible hindsight are not persuasive because **Zeldis teaches a limited list of fillers** [] (talc, calcium carbonate, microcrystalline cellulose, cellulose, dextrates, kaolin, mannitol, silicic acid, sorbitol, starch, pregelatinzed starch, and mixtures thereof), **a limited list of disintegrants** [] (agar-agar, alginic acid, calcium carbonate, microcrystalline cellulose, croscarmellose sodium, crospovidone, polacrilin potassium, sodium starch glycolate, potato starch, tapioca starch, starches, pre-gelatinized starch, clays, algins, celluloses, gums, and mixtures thereof), and **a limited list of lubricants** []. It would have been obvious to have formed a solid dosage form comprising pamolidomide [sic] in any combination of filler(s), binder(s), and

> lubricant(s) as described by Zeldis. Zeldis teaches ranges of concentrations of the components and it would have been obvious to have varied the amounts of components within the taught ranges. A person of ordinary skill in the art would have arrived at the claimed invention through **routine experimentation** and it would have been **obvious** to have formed a solid dosage form from any possible combination of excipients disclosed by Zeldis.
>
> (emphasis added).

231. Meanwhile, would be generic makers had been developing their products. On February 8, 2017—the first date on which ANDA applicants could file an application for generic pomalidomide—at least seven generic manufacturers (Teva, Natco/Breckenridge, Apotex, Hetero, Par, Aurobindo, and Mylan) filed ANDAs to market generic Pomalyst.

232. In the following months, some ANDA applicants provided information to Celgene about their ANDA products, including how some ANDA applicants had formulated their versions of generic pomalidomide.

233. By September of 2017, Celgene had a plan as to how to modify the pending formulation claims to increase the scope of the previously approved formulation claims (and thereby increase the potential for infringement by would-be competitors) while at the same time potentially persuade the examiner to issue a patent.

234. On September 21, 2017, an interview was conducted between the patent examiner and Celgene's representatives, during which Celgene represented that it could supply a declaration showing unexpected stability results.

235. On October 20, 2017, Celgene amended the claims to add a requirement that the starch to mannitol ratio be from 1:1 to 1:1.5. And on February 22, 2018, Celgene submitted yet another response and a new declaration by Tutino.

236. The February 2018 Tutino declaration was false and misleading. First, the declaration presents undated stability test results of six formulations of pomalidomide (0.5 mg, 1.0 mg, 2.0 mg,

3.0 mg, 4.0 mg and 5.0 mg) and falsely states the stability results are surprising and unexpected. It was well known and well documented in the prior art that thalidomide and its analogs such as pomalidomide posed stability issues, which a person skilled in the art would have been aware of in conducting the type of routine experimentation that led to the claimed invention. And the techniques to achieve stable formulations of such compounds were also well known. Second, the formulations presented used only two close ratios of starch to mannitol (*i.e.*, 1:1.30402385 and 1:1.33069307) and did not support the range claimed by Celgene (*i.e.*, 1:1.0 to 1:1.5).

237. On March 15, 2018, the examiner allowed the '467 formulation patent to issue, subject to a terminal disclaimer as to the '427 patent.

238. The '467 patent would not have issued absent the deceptive declarations submitted by Tutino during the patent prosecution. The second Tutino Declaration repeats the same fraudulent representations as the first Tutino Declaration regarding "unexpectedly" encountering and addressing stability issues, which Tutino supplements in his second declaration with undated testing data. There would have been nothing surprising about the well-known fact that thalidomide analogs are unstable due to hydrolysis, an issue that would be addressed through standard, routine optimization. Tutino misled and deceived the patent examiner when he suggested otherwise. The examiner justifiably relied on the deceptive Tutino declarations, allowing the patents to issue based on the submission of the Tutino declarations after repeated prior rejections of the claims.

239. In addition to being unenforceable, the '467 is invalid for obviousness and, in any event, is very limited in scope. During the patent prosecution (during which Celgene saw its claims rejected four separate times), Celgene was forced to narrow the claims substantially. As issued, the '467 has one independent claim, which claims:

> An oral dosage form in the form of a capsule which comprises: 1) pomalidomide at an amount of 0.1 to 3 weight percent of the total weight of the composition; 2) a binder or filler at an amount of 90 to 99 weight percent of total weight of the composition, wherein the

> binder or filler is a mixture of starch and mannitol; and wherein the ratio of mannitol: starch in the dosage form is from about 1:1 to about 1:1.5 . . . .

240. Thus, even if the patent was valid, it is highly unlikely Celgene would be able to prove infringement. The '467 does not claim any kind of complexity, such as bioequivalence metrics, that would require a generic manufacturer to do extensive testing to ascertain whether its formulation would infringe. Instead, the patents are more akin to a recipe, identifying a finite list of ingredients (primarily pomalidomide, starch, mannitol, and sodium stearyl fumarate) combined in certain specified amounts or ratios. A generic manufacturer would be able to design around these patents to produce a non-infringing product, for example, by adjusting the ratios or by using different binders/fillers, while still maintaining the desirable features, such as stability and bioavailability.

I. In February 2017, numerous generic manufacturers filed generic Pomalyst ANDAs, leading to the first wave of patent infringement lawsuits by Celgene.

241. Because the FDA had first approved Pomalyst on February 8, 2013, under regulations governing new chemical entity exclusivities, the first date upon which a generic company could file an ANDA for generic Pomalyst was February 8, 2017 (four years after approval, if challenging patents). In such situations, it is not uncommon to see multiple generics all file on the first available date.

242. On February 8, 2017, at least seven generic manufacturers (Teva, Natco/Breckenridge, Apotex, Hetero, Par, Aurobindo, and Mylan) filed ANDAs to market generic Pomalyst.[92] These generics all sought first-to-file status, with the potential for the 180-day exclusivity so long as they obtained timely tentative or final drug approval.

[92] The final approval letters for Natco/Breckenridge and Aurobindo state that the filing dates for these ANDA is February 8, 2017. The final approval letter for Mylan is not publicly available. CenterWell inferred that the Mylan ANDA, as well as the Teva, Apotex, Hetero, and Par ANDAs

243. At least nine ANDAs have been filed to date[93], listed here.

Generic	ANDA No.
Teva	209956
Natco/Breckenridge	210111
Apotex	210164
Synthon/Alvogen	210232
Hetero	210236
Par	210245
Aurobindo/Eugia	210249
Mylan	210275
Dr. Reddy's	213234

244. In late March/early April 2017, Celgene received seven paragraph IV letters from the ANDA filers certifying that Celgene's Pomalyst patents were either invalid and/or would not be infringed by the manufacturer's ANDA product.

245. On May 4, 2017, Celgene filed its first Pomalyst patent infringement lawsuit. The suit, against Par and Teva, alleged infringement of four patents. On May 11, 2017, Celgene sued Hetero, Aurobindo/Eugia, Apotex, Mylan, and Natco/Breckenridge, for infringement of the same four patents:

8,198,262	Method of treatment
8,673,939	Method of treatment
8,735,428	Method of treatment
8,828,427	Formulation

246. All four of the asserted patents were unenforceable due to Celgene's fraud on the patent office, invalid as obvious over the prior art, and, in the case of at least the '427, subject to strong non-infringement arguments. However, by simply filing these patent lawsuits, Celgene

were also filed on February 8, 2017, based in part of the dates the paragraph IV letters were sent (as disclosed in Celgene's complaints against these entities).

[93] In 2018 and 2019, Synthon/Alvogen and DRL, respectively, filed ANDAs.

triggered an automatic 30-month stay, which was extended to August 8, 2020 (*i.e.*, 7.5 years after NDA approval) due to the NCE exclusivity. During this time, the FDA was barred from granting final approval to any ANDA.

1. Celgene's lawsuits alleging infringement of the Pomalyst method of treatment patents (the '262, '428, '3939) and the only then-existing formulation patent (the '427) were a sham.

247. Celgene's infringement lawsuit was objectively and subjectively baseless. A reasonable pharmaceutical company in Celgene's position could not realistically expect to succeed on the merits of its lawsuits alleging infringement of the method of treatment patents and the '427 formulation patent.

248. All four patents were obtained through fraud on the patent examiner and were therefore unenforceable. Because Celgene's fraudulent and deceptive conduct would have been revealed during the patent litigation, Celgene could not have expected that it would prevail in the patent infringement litigation.

249. There was no objective basis for asserting that the method of treatment patents were valid and infringed for the additional reason that the patents were clearly obvious over the prior art, which taught: (1) a method of using pomalidomide to reduce TFNα and that reduction of TNFα is an effective cancer treatment (the '517); (2) the use of pomalidomide specifically to treat multiple myeloma and/or relapsed/refractory multiple myeloma (D'Amato (2001), Davies (2001), Lentzsch (2001), Lentzsch (2002), Schey (April 2002), and Schey (October 2002)); (3) the maximum tolerated daily dosage of pomalidomide (Schey (April 2002)); (4) the clinical efficacy of dexamethasone with thalidomide to treat resistant multiple myeloma (Weber (2000)); (5) the specific amount of dexamethasone claimed (40 mg) combined with thalidomide to treat multiple myeloma (Coleman (2002)); (6) the cyclical treatment of multiple myeloma (Kyle (2001)); (7) the specific 28-day dosing cycle, *i.e.*, 21 days administration of an anticancer drug followed by 7 days of rest, in combination

with dexamethasone (Cohen (1982)); (8) thalidomide and its analogues ability to overcome drug resistance of multiple myeloma cells (Hideshima (2000)); and (9) that pomalidomide is a more potent agent with decreased potential for birth defects (Corral (1999)).

250. The '427 formulation patent was similarly invalid as obvious over the prior disclosures, claiming an invention that was not, in fact, novel, but the result of routine optimization.

251. Even if the formulation patents were somehow valid, a brand company in Celgene's position could not reasonably expect to prove that the '427 was infringed. The '427 is a simple patent claiming a finite combination of ingredients and weights. Generic companies routinely design around formulation patents like the '427 to avoid infringement. Celgene had so little confidence in the '427 patent, it would end up withdrawing its infringement claims as to this patent before most, if not all, of the settlements occurred.[94]

252. If litigated to a decision on the merits, these patents (the '262, '428, '3939, and '427) would be adjudged unenforceable, invalid, and/or not infringed for the reasons given above. Celgene pursued the litigation, not because it had an expectation of achieving a favorable outcome, but rather to use the litigation process itself to impede generic entry. By simply filing the lawsuit, Celgene obtained an automatic 30-month delay during which the FDA could not grant final approval to any generic Pomalyst product.

2. Throughout 2017, the generic manufacturers aggressively defended against Celgene's claims of infringement, with some generics filing counterclaims against Celgene.

253. After Celgene instituted its patent infringement litigation campaign, the generic manufacturers filed answers stating that the asserted patents either would not be infringed by the generic's ANDA product or were invalid. Several of the generic manufacturer defendants also

[94] *See Celgene v. Hetero,* 17-3387 (D.N.J.), Special Discovery Master Order No. 14 dated Dec. 31, 2020 at n.1 (ECF 821) ("Celgene is not asserting the '427 patent against defendants.").

asserted counterclaims against Celgene. Celgene filed answers as to these counterclaims and in some instances filed counter-counterclaims, which precipitated another round of answers. The filing of these pleadings occupied much of 2017 and early 2018. One generic manufacturer, Mylan, took a different tact. On August 8, 2017, Mylan filed a motion to dismiss for, *inter alia,* improper venue. The court did not initially grant the motion and instead allowed the parties to engage in venue related discovery.

254. During this time, Celgene continued to work on all fronts to extend its monopoly. On July 17, 2017, the examiner granted a final determination of a patent extension for the '262 patent, moving the original expiry date from October 19, 2024, to June 17, 2025.

255. As of the end of 2017, Celgene was litigating infringement claims as to four patents (the three method of treatment patents and one formulation patent) and it was in the process of prosecuting the patent application that would eventually lead to the '467 formulation patent.

256. On December 17, 2017, the would-be generic companies filed a nearly two-hundred-page statement of invalidity contentions regarding the '262, '3939, '428, and '427 patents.

J. Throughout 2017-2018, Celgene continued to fraudulently obtain patents.

257. Aware of the weaknesses of its '262, '3939, '428, and '427 patents, Celgene sought to bolster its generic blockade by acquiring even more patents.

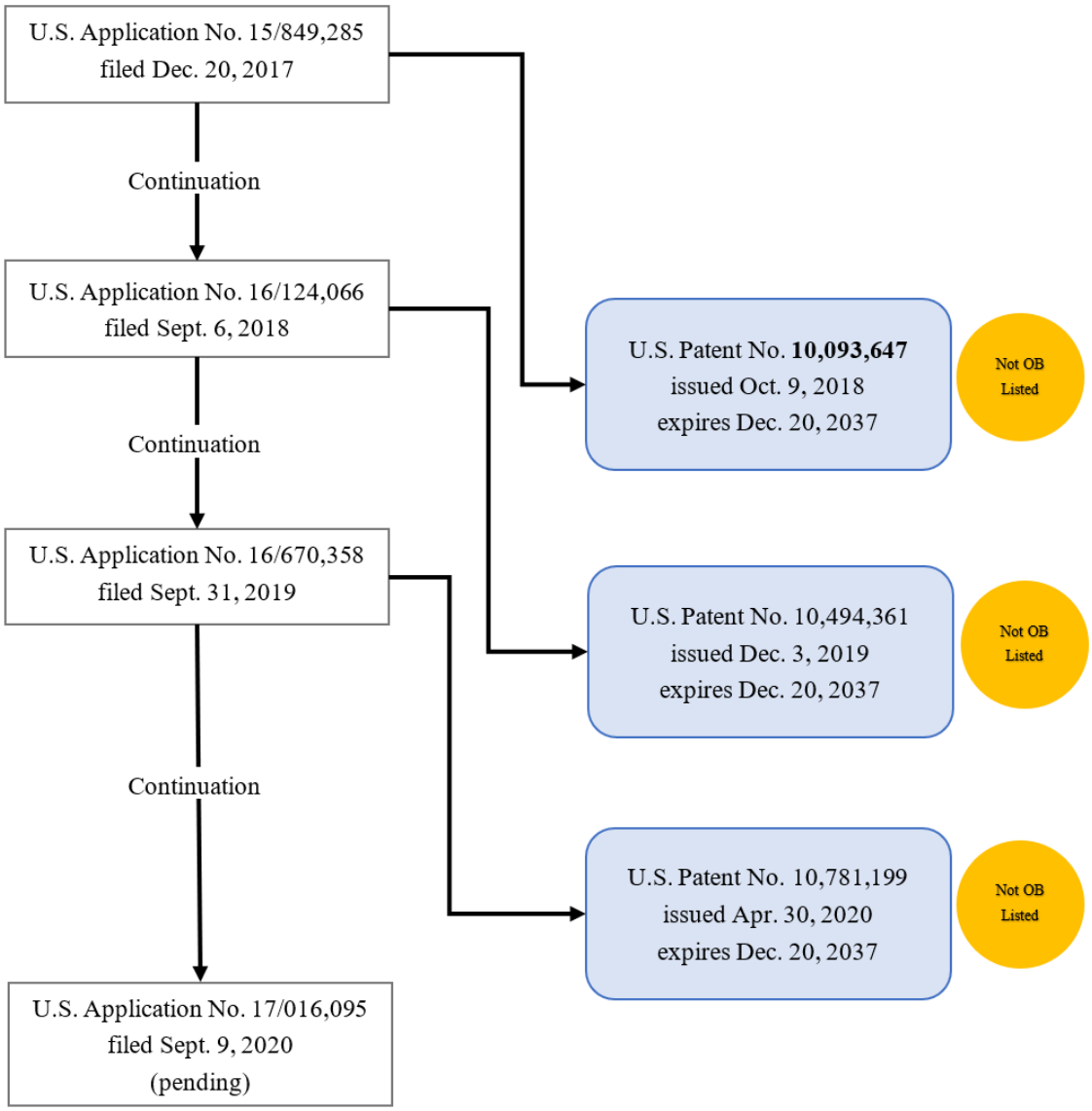
1. In late 2017, approximately nine months after receiving the paragraph IV letters, Celgene sought three new patents claiming polymorphic forms (the '647, '648, and '649).

258. On December 20, 2017, Celgene[95] filed three new patent applications claiming polymorphs[96], which would ultimately lead to the '647, '648, and '649. Each of these patents derives from a separate patent application:

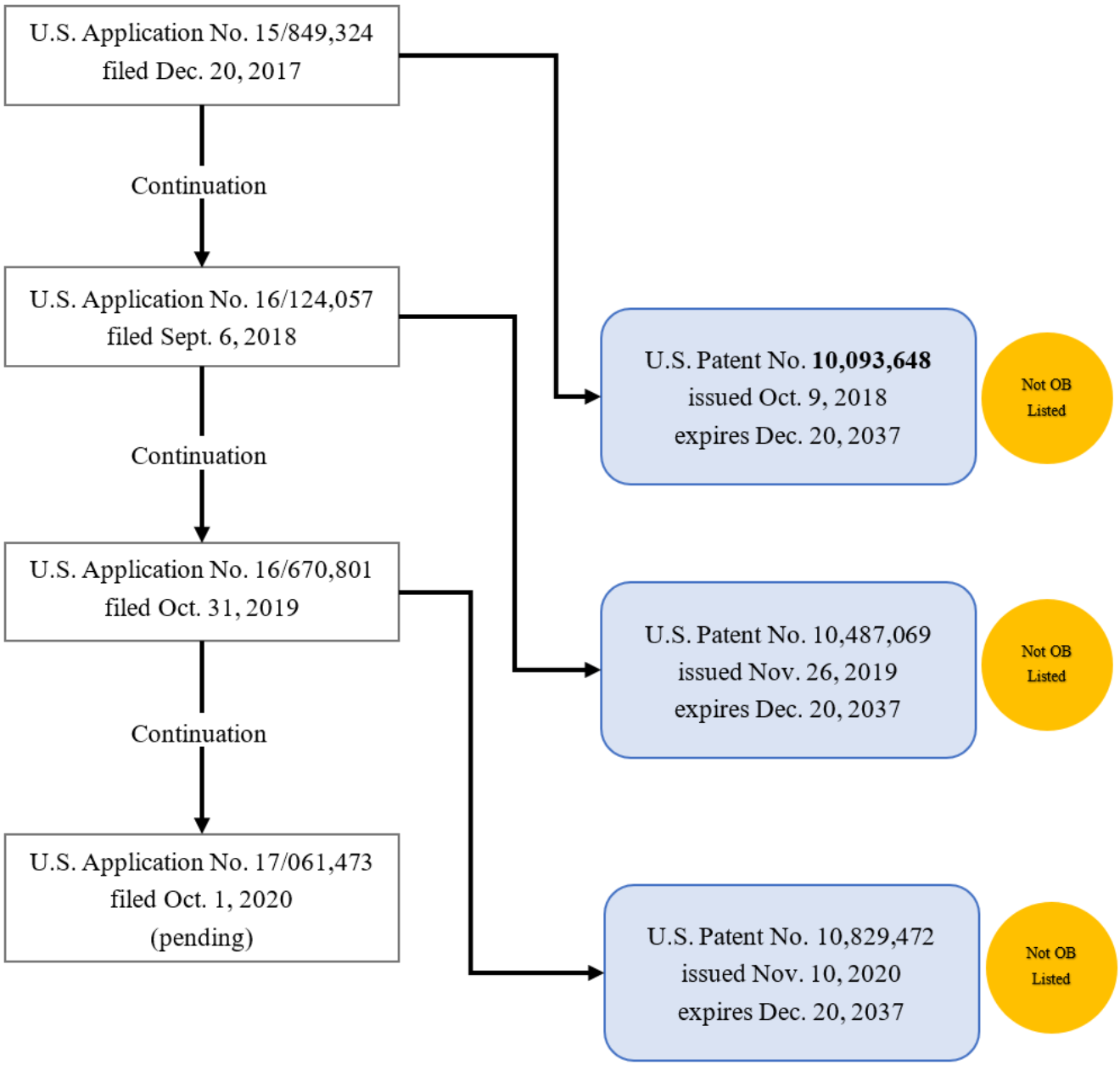
[95] The named inventor is Jerry Atwood, who subsequently assigned the patents to Celgene. To avoid confusion, the applicant for the polymorph patents is referred to here simply as "Celgene."

[96] Polymorphism refers to the ability of a chemical compound to crystallize into different three-dimensional crystal structures.

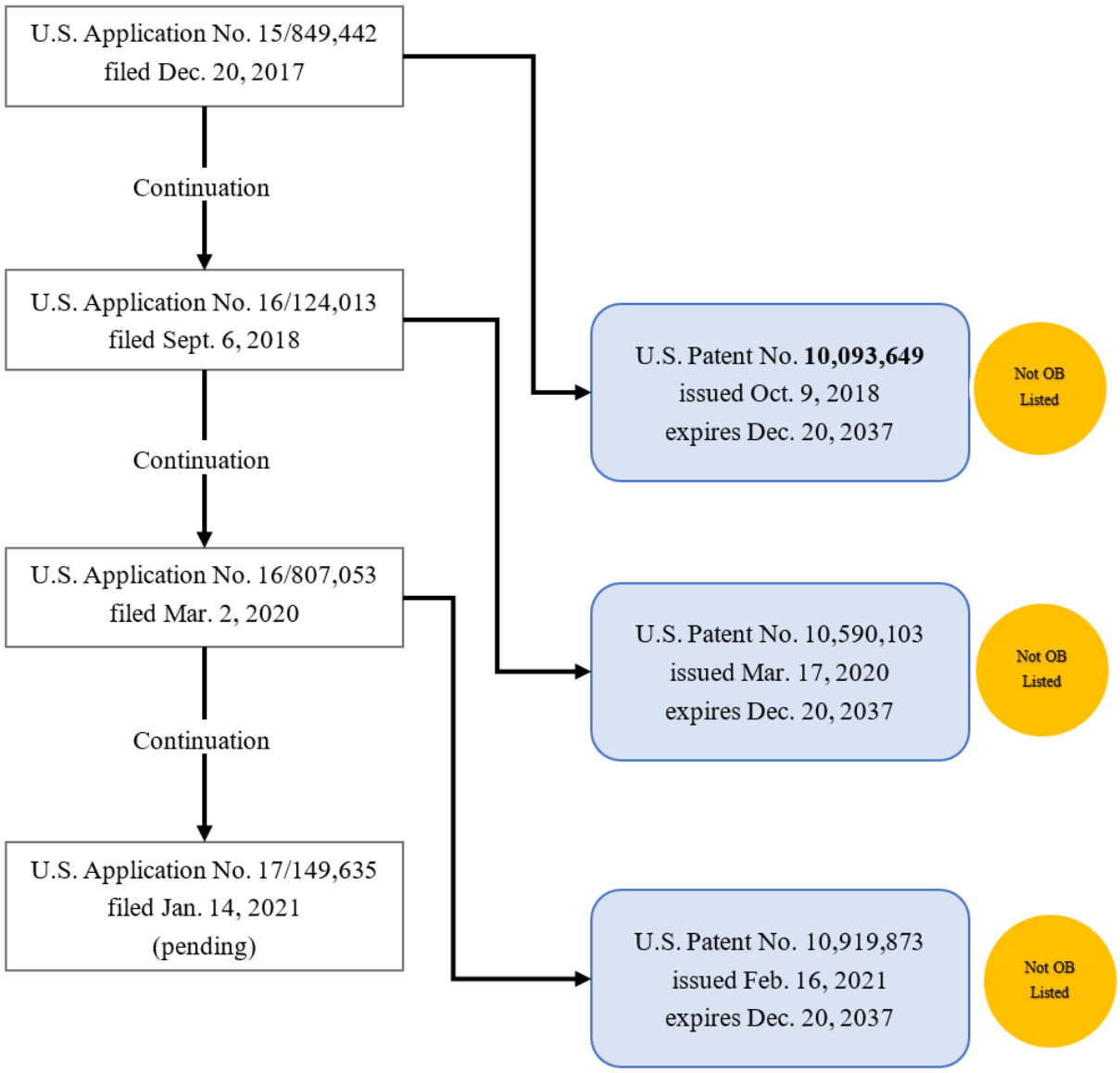
'285 PATENT APPLICATION TREE



'324 PATENT APPLICATION TREE



'442 PATENT APPLICATION TREE



259. The priority date for each of these patents post-dates the majority of the first filers' Paragraph IV letters, which were transmitted in March and April 2017:

Patent	Application Date	Priority Date
'647	12/20/2017	5/26/2017

Patent	Application Date	Priority Date
'648	12/20/2017	9/22/2017
'649	12/20/2017	9/22/2017

260. Each of Celgene's polymorph patents has a single independent claim, claiming a crystalline form identified by an x-ray powder diffraction pattern ("XRPD") with specific peaks. An XRPD is like a thumbprint for crystalline forms.

261. For example, the '647 claims "Crystalline 4-amino-2-(2,6-dioxopiperidine-3-yl) isoindoline-1,3-dione dihydrate, having an X-ray powder diffraction pattern comprising peaks at 13.9, 16.6, and 25.5 degrees 2θ±0.2 degrees 2θ." The identification of those peaks helps to identify the specific polymorphic form at issue. The Pomalyst polymorph patents are further limited to three specific hydrate forms of pomalidomide: dihydrate ('647); hemihydrate ('648); and monohydrate ('649).

262. Celgene applied for these three patents approximately nine months after receiving seven paragraph IV letters, which described the generic Pomalyst ANDA products in detail. It strains credulity that these patents could be both infringed by an earlier-in-time ANDA product and simultaneously novel over the prior art. Celgene applied for these patents to create additional hurdles for generics, rather than for any legitimate purpose.

2. In the Spring of 2018, Celgene pursued the '5939 formulation patent through fraud.

263. Celgene's quest to acquire additional Pomalyst patents to block generic competition continued. On May 10, 2018, Celgene filed application no. 15/976,808. Celgene filed this patent application more than a year after receiving seven paragraph IV letters describing in detail the ANDA products those generic manufacturers sought to bring to market:

Generic manufacturer	Date of paragraph IV letter
Teva	March 30, 2017

Generic manufacturer	Date of paragraph IV letter
Natco/Breckenridge	April 11, 2017
Apotex	March 30, 2017
Hetero	March 29, 2017
Par	April 12, 2017
Aurobindo	April 5, 2017
Mylan	April 6, 2017
Synthon/Alvogen	May 4, 2018
DRL	May 31, 2019

264. Patent application no. 15/976,808 would eventually lead to the 10,555,939. The '5939 is identical to the '467, except that the '5939 claims slightly broader ranges as compared to the '467 in two claims:

Claim no. (type)	'467	'5939
1 (independent)	1. An oral dosage form in the form of a capsule which comprises: 1) pomalidomide at an amount of 0.1 to 3 weight percent of the total weight of the composition; 2) a binder or filler at an amount of **90** to 99 weight percent of total weight of the composition, wherein the binder or filler is a mixture of starch and mannitol; and wherein the ratio of mannitol: starch in the dosage form is from about 1:1 to about 1:1.5.	1. An oral dosage form in the form of a capsule which comprises: 1) pomolidomide at an amount of 0.1 to 3 weight percent of the total weight of the composition; 2) a binder or filler at an amount of **70** to 99 weight percent of total weight of the composition, wherein the binder or filler is a mixture of mannitol and starch; and wherein the ratio of mannitol:starch in the dosage form is from about 1:1 to about 1:1.5.
3 (dependent)	3. The oral dosage form of claim 1, wherein the binder or filler is present at an amount of 95 to 99 weight percent of total weight of the composition.	3. The oral dosage form of claim 1, wherein the binder or filler is present at an amount of 85 to 99 weight percent of total weight of the composition.

265. During the prosecution of this formulation patent, Celgene again tried to define the scope of the claims broadly, as it did with the prior formulation patent applications. The examiner

rejected the patent application four separate times as obvious over the prior art (*i.e.*, Zeldis, Remington's, and McNally) and for double patenting.

266. Celgene again sought to overcome the examiner's obviousness rejections by resubmitting the June 17, 2013 Tutino Declaration and claiming "unexpected results." During the prosecution of the '5939, the patent examiner specifically stated that the argument regarding "unexpected results" was not persuasive: "Applicant's arguments related to unexpected results were fully considered but are not persuasive for reasons of record."

267. The patent examiner ultimately allowed the patent to issue after Celgene filed a terminal disclaimer as to the '427 and '467.

268. The '5939, which was nearly identical to the '467 (differing only as to the ranges in two discrete respects), is invalid as obvious over the prior art and (as with the other formulation patents) was exceedingly easy to design around.

3. In June 2018, Celgene obtained the '467 formulation patent by fraud, prompting Celgene to file a new wave of sham litigation.

269. On June 12, 2018, the '467 formulation patent issued. Although this patent did not issue until more than a year after the ANDA filings, Celgene nevertheless promptly filed new lawsuits against the generic manufacturers alleging infringement of this newly-issued patent:

Generic Manufacturer	Date Sued For Infringement of the '467
Teva	September 27, 2018
Breckenridge and Natco	October 5, 2018
Hetero	October 9, 2018
Mylan	November 11, 2018
Apotex	November 21, 2018
Aurobindo	January 4, 2019

270. Although the generics would be forced to defend against Celgene's '467 infringement claims, the filing of those lawsuits could not trigger an automatic 30-month stay as to eight of the

ANDAs, as the '467 did not exist at the time those ANDAs were filed. Thus, the filing of these lawsuits could not prevent the FDA from granting final approval. The filing of the '467 infringement litigation therefore could not have prevented an at-risk launch. Nor would the '467 have deterred an at-risk launch under competitive conditions, as the patent was invalid and easily designed around.

271. A reasonable litigant in Celgene's position could not realistically expect to prevail on the merits of its lawsuits alleging infringement of the '467. The patent was obtained through the fraudulent Tutino declarations, which would have been revealed during the adversarial process in the patent litigation. The patent would have been found to be invalid over the prior art. Celgene had no hope of proving that any generic's ANDA product, let alone all of the ANDA products, would infringe this very narrow, easy to design around patent. Celgene did not pursue the litigation with any expectation of achieving a favorable outcome. Instead, Celgene's lawsuit was motivated by the intent to use the litigation process itself to delay generic competition by creating hurdles for the generics.

K. Throughout 2018-2019 Celgene continued to file sham patent infringement lawsuits against generic manufacturers.

1. In mid-2018, Celgene also filed patent infringement litigation against the later ANDA filer Synthon/Alvogen.

272. In May 2018, Synthon and Alvogen, which had partnered on a Pomalyst ANDA, sent their Paragraph IV letter to Celgene. Because Synthon/Alvogen were not first-filers (most generics sent their Paragraph IV letters in February 2017, approximately fifteen months earlier), Synthon/Alvogen would be precluded from entering the market until expiration of any 180-day exclusivity period awarded to (and shared by) the first-filers.

273. On June 19, 2018, Celgene filed suit against Synthon/Alvogen for infringement of four of the Pomalyst patents: the '267, '3939, '428, and '427. In November 2018, Celgene filed an amended complaint adding infringement claims as to the '467 patent.

274. For the same reasons as stated earlier, a brand company in Celgene's position could not realistically expect to prevail on the merits in this infringement lawsuit, but nonetheless filed the lawsuits with the intent to use the judicial process itself to impede generic entry by Synthon/Alvogen.

2. In November 2018, the parties filed their Opening Claim Construction briefs, previewing arguments on which Celgene's infringement claims would rise and fall.

275. On November 15, 2018, the parties filed their Opening Claim Construction briefs regarding the four patents Celgene initial sued on (the '262, '428, '3939, and '427).

276. As relevant to the three method of treatment patents, Celgene conceded that "***Patentability of the claimed methods depends upon efficacy***." Celgene was clear in this position, reiterating the point multiple times in its briefing:

- "[T]he examiner allowed the claims to issue over the prior art because the claimed methods were shown to be efficacious against MM when another therapy failed. In requiring evidence of efficacy to allow the claims to issue, the Examiner confirmed that efficacy is a required part of the claimed inventions."
- "Defendants seek to read efficacy – the very crux of the invention – out of the claims."
- "Here, '[a] method of treating multiple myeloma' requires efficacy against MM. If not, then the invention would lose its entire purpose. That is neither what the inventors intended, or what the intrinsic evidence shows."
- "Adopting Defendants' position that the preamble is not limiting, and therefore does not require efficacy, would negate the purpose of the claimed inventions."
- "[H]ere, efficacy against MM is a fundamental feature of the claimed invention."
- "Without a limiting preamble [claiming efficacy], the 'invention would have no purpose.'"

- "[H]ere, the preamble – 'a method of treating multiple myeloma' – is limiting because it is the basis upon which the Patent Office allowed the claims. The Examiner allowed each of the MM patents to issue specifically because the inventions claimed therein demonstrated efficacy against MM."

- "[T]he claims issued only because the inventors demonstrated to the Examiner that their invention was efficacious against MM."

- "Because the prosecution history makes clear that the claims would not have issued absent evidence that the claimed methods resulted in efficacy against MM, which is conveyed through the preamble, the Court should construe "a method of treating multiple myeloma" as a claim limitation."

277. As the generic manufacturers explained in their Opening Claim Construction Brief, "Celgene seeks such a limiting construction so that it may argue during the merits phase of this case, incorrectly, that [the generic manufacturer defendants'] prior art does not anticipate or render obvious the asserted [method of treatment] patent claims because the prior art allegedly did not disclose that administration of pomalidomide would be efficacious in treating multiple myeloma."

3. In late 2018 to early 2019, Celgene obtained the polymorph patents and promptly filed additional new sham litigation as to those three patents.

278. On October 9, 2018, the three polymorph patents (the '647, '648, and '649) issued. Celgene had not even applied for the polymorph patents until months after receiving the ANDA filers' paragraph IV letters. Celgene nevertheless promptly filed new lawsuits against the generic manufacturers alleging infringement of the newly issued polymorph patents ('647, '648, and '649):

Generic Manufacturer	Date sued for infringement of the polymorph patents
Mylan	February 14, 2019
Hetero	February 14, 2019
Natco/Breckenridge	February 14, 2019
Apotex	February 14, 2019
Teva	March 19, 2019
Synthon/Alvogen	April 12, 2019

279. Celgene's claims of infringement were doomed from the start by a catch-22 of Celgene's own making: if an earlier-in-time ANDA product would infringe one of Celgene's later-in-time polymorph patents, then the patent is invalid as anticipated and/or obvious in light of the prior art.[97]

280. Even if the polymorph patents were somehow valid, it is impossible that Celgene could prove all nine of the differing ANDA products infringed these three patents. To block generic entry based on the polymorph patents, Celgene would be required to establish that all nine ANDA products were a dihydrate, hemihydrate, or monohydrate exhibiting the same x-ray diffraction patterns with the same peaks as those claimed in the patents. Even if Celgene could overcome the serious invalidity issues described above, Celgene could not succeed in proving that all (or even most) of the generic ANDA products possessed the very specific x-ray diffraction patterns claimed by the polymorph patents.

281. A brand company in Celgene's position could not realistically expect to prevail on its claims that the polymorph patents were valid and infringed. Celgene filed the litigation with the purpose and the intent to create yet another hurdle to impede generic entry.

4. In the Spring of 2019, Celgene sued to block the entry of Dr. Reddy's, a new generic manufacturer that sought to enter the market with generic pomalidomide.

282. On March 29, 2019, Dr. Reddy's filed an ANDA for generic Pomalyst. Like Synthon/Alvogen, Dr. Reddy's was not one of the first filers and therefore would not be able to enter the market with generic Pomalyst until after expiration of any 180-day exclusivity period awarded to the first filers.

[97] *See* 35 U.S.C. §§ 102, 103.

283. On May 31, 2019, Dr. Reddy's sent written notice of its paragraph IV certification to Celgene.

284. On July 12, 2019, Celgene sued Dr. Reddy's for infringement of the '262, '3939, '428, '427, and '467.

285. For the same reasons as discussed earlier, a brand company in Celgene's position could not realistically expect to prevail on the merits in this infringement lawsuit. Celgene nonetheless filed the lawsuits with the intent to use the judicial process itself to impede generic entry by Dr. Reddy's.

L. In August 2019, the first-to-file generic manufacturers missed a regulatory deadline that put them at risk of forfeiting their 180-day exclusivity.

286. To avoid forfeiture of the right to the 180-day statutory exclusivity, the group of generic companies—Teva, Natco/Breckenridge, Apotex, Hetero, Par, Aurobindo, and Mylan—that had filed their ANDAs on the first available date (February 8, 2017) were required (subject to a rare exception) to obtain tentative or final approval of their application from the FDA by August 8, 2019.

287. However, by August 8, 2019, none of the first filers had received tentative approval. The FDA (in later regulatory filings) had noted the failure to do so, but the FDA left for later determination a final decision on whether forfeiture had occurred.

288. As a result, all of the first filing generics were at significant risk of having forfeited their 180-day exclusivity.

M. In February 2020, Celgene obtained the '5939 formulation patent by fraud, leading Celgene to initiate yet another wave of sham litigation.

289. On February 11, 2020, the '5939 formulation patent issued. Although this patent did not exist until *three years after* the ANDAs were filed, Celgene nevertheless initiated another new wave of patent litigation, filing substantially identical complaints alleging infringement of the '5939 against

the following generic manufacturers on March 10, 2020: Apotex; Natco/Breckenridge; Hetero; Aurobindo; Mylan; Teva.

290. The '5939, a continuation of the '427 and '467 formulation patents, is invalid as obvious considering the prior art, including Zeldis, Remington's, and McNally. The patent examiner expressly stated it was not persuaded by the Tutino Declaration's assertion of "unexpected results." The '5939 only issued after Celgene filed a terminal disclaimer as to the '427 and '467. As with the other Pomalyst formulation patents, the '5939 was also exceedingly easy to design around.

291. The '5939 litigation was subjectively and objectively baseless. Celgene could not hope to prevail on its infringement claims regarding this patent. As with the '427 and '467, the '5939 was a simple patent that generics would readily design around to avoid infringement. With nine different generics seeking to bring generic Pomalyst to market, Celgene could not expect to prove that any one, let alone all nine, ANDA products infringed this simple patent.

292. Even if Celgene could prove infringement, it knew that its family of formulation patents were obtained based on the fraudulent Tutino declarations and unenforceable. Celgene pursued the litigation, not because it had a reasonable expectation of prevailing on the merits, but with the intent to impede and prevent generic competition.

N. In 2020, Celgene's campaign to block generic competition suffered a series of losses, as the generic manufacturers scored key wins in the patent litigation.

293. By Spring 2020, the original Pomalyst patent litigation had been pending for approximately three years. During this time, the parties filed several briefs related to claims construction, *i.e.*, determining the definitions of disputed patent terms. In addition, Mylan and Celgene had engaged in venue related discovery and, on April 13, 2020, Mylan renewed its motion to dismiss for, *inter alia,* improper venue.

294. On June 16, 2020, the court issued its Claim Construction Order.[98] The order addressed four disputed terms in the three method of treatment patents (the '262, '428, and '3939) and the three formulation patents (the '427, '467, and '5939).

295. With respect to the method of treatment patents, the parties disputed *inter alia* whether the preamble of the method of treatment claims, specifically the phrase "A method of treating multiple myeloma," should be construed as limiting the claims.[99] Celgene argued that "the phrase 'treating multiple myeloma' in the preamble limits the claim by requiring efficacy in patients who received pomalidomide."[100] The generic manufacturers argued that the claims were not limited to the efficacious treatment of multiple myeloma, claiming only the administration of the compound as described in the claims.

296. The dispute was of critical significance to the validity of the method of treatment patents, as Celgene would argue at the merits phase of the case that the claimed invention was not anticipated or obvious over the prior art because the prior art did not disclose that pomalidomide would be efficacious in the treatment of multiple myeloma. In its effort to persuade the court that the method of treatment patents were limited to the *efficacious* treatment of multiple myeloma, Celgene argued that the "[p]atentability of the claimed methods depends upon efficacy."[101]

297. The court rejected Celgene's interpretation, agreeing with the generic manufacturers that the method of treatment claims were not limited to the *efficacious* treatment of multiple myeloma: "While the Court agrees that the dispute term, 'treating multiple myeloma,' must be construed in its

[98] *Celgene v. Hetero,* No. 17-3387, 2020 WL 3249117, *2 (D.N.J.) (ES)(MAH).

[99] *Id.* at *4.

[100] *Id.*

[101] *Celgene v. Hetero,* No. 17-3387 (D.N.J.), Celgene Opening Markman Brief, at 11; *see also* ¶ 242, *supra.*

entirety, *nothing in the claim language, the specification, or the prosecution history warrants reading into the claim an efficacy limitation based on the preamble.*"[102]

298. The ruling eliminated any doubt that the method of treatment patents are invalid, as Celgene itself had conceded that patentability depended upon the claims being limited to the efficacious treatment of multiple myeloma.

299. Shortly after the court's *Markman* Decision, it dismissed Celgene's complaint against Mylan for improper venue.[103]

O. Fall of 2020: Generic entry for pomalidomide was imminent.

300. As 2020 continued, Celgene suffered additional setbacks in its generic exclusion campaign.

301. By the fall of 2020, generic entry for pomalidomide in the United States was imminent.

302. First, the NCE exclusivity period for Pomalyst had long since expired (in February 2018). As a result, the FDA was not barred to granting final approval due to NCE exclusivity.

303. Second, as to those generic companies who shared first-to-file ANDA status (having all filed on the first available date of February 8, 2017), the 30-month stay of ANDA approval passed in August of 2020. As a result, there was no longer a regulatory bar to the FDA granting final approval for generic Pomalyst.

304. Third, in October 2020, five of Celgene's Orange Book listed patents (the REMS patents) expired, eliminating any arguable issues that those patents could prevent generic entry.

305. Fourth, on October 30, 2020, FDA granted final approval to the Aurobindo and Natco/Breckenridge ANDAs. This meant that there were no longer any FDA-imposed regulatory

[102] *Id.* at *5 (emphasis added).

[103] *Celgene v. Mylan,* No. 19-cv-5802, 2020 WL 12570814 (D.N.J. Sept. 25, 2020).

barriers preventing Aurobindo or Natco/Breckenridge from launching its generic product immediately.[104]

306. Fifth, Celgene's Pomalyst patent portfolio was riddled with fraudulently obtained patents, patents that were in all likelihood going to be held invalid or not infringed in the various sham lawsuits Celgene had filed.

307. Sixth, market dynamics presented a significant likelihood of imminent generic entry for any generic company. Pomalyst was selling over $2 billion a year, making it a highly desirable market for generic entry. While both Natco/Breckenridge and Aurobindo shared first-to-file status with other generics, those other generics had not yet received final FDA approval, opening an opportunity of *de facto* generic exclusivity for the first entrant or entrants. And while entry before conclusion of the patent litigation would require at-risk entry, those risks here were minimal (if not non-existent), and at-risk entrants, in any event, almost invariably pay less in damages than what they earn during at-risk launch.[105]

308. In short, as early as of October 2020, Celgene faced imminent pomalidomide generic competition which would have cratered its $2 billion Pomalyst franchise.

[104] Whether these generics would be entitled to the 180-day exclusivity period was an open question. As FDA noted in the final approval letters, Aurobindo and Natco/Breckenridge had failed to get tentative approval within 30 months of filing its ANDA, potentially jeopardizing their 180-day exclusivity period. FDA deferred a decision on the 180-day exclusivity question until such time as another first filer became eligible for final approval.

[105] Keith M. Drake, Robert He, Thomas McGuire, and Alice K. Ndikumana, *No Free Launch: At-Risk Entry by Generic Drug Firms*, NBER Working Paper No. 29131, August 2021, JEL No. D22, I11, I18,O32, available at https://www.nber.org/system/files/working_papers/w29131/w29131.pdf (last accessed August 21, 2024).

P. Celgene and BMS paid off its would-be pomalidomide competitors.

309. Rather than allow lawful competition in the U.S. market for pomalidomide, starting in November 2020, Celgene and BMS began a serial scheme to pay off its would-be pomalidomide competitors to have them delay generic entry for about six years, until early 2026.

1. November 2020: The Celgene-Natco reverse payment agreement.

310. In about late October or early November 2020, Celgene and BMS (which had acquired Celgene by this point, as discussed earlier in the Complaint), on the one hand, and Natco and Breckenridge, on the other, settled the pending pomalidomide litigation between them (the "Celgene-Natco agreement") under terms that provided for a large, unjustified payment from Celgene/BMS to Natco/Breckenridge. In return, Natco/Breckenridge agreed to delay entry into the U.S. pomalidomide market until six years later, *i.e.*, on a date strategically timed such that all the first filing generics would have the same agreed entry date—the first quarter of 2026.

311. The Celgene-Natco agreement does not represent a *bona fide*, arms-length resolution of the merits of the pomalidomide litigation.

312. *First*, the facts of the existing patents and litigation show that the Celgene-Natco agreement is not based on the merits of the patent dispute; Natco/Breckenridge had little reason to settle, and certainly not on terms where market entry is delayed until early 2026.

313. At the time, Celgene had nine unexpired pomalidomide patents: the three method of treatment patents ('262, '3939, '428), the three polymorph patents ('647, '648, '649), and the three formulation patents ('427, '467, '5939).

314. As to the three method of treatment patents, Celgene had no colorable basis to prosecute to conclusion infringement litigation based on them (as previously alleged), and all three were to expire *before* the agreed entry date (the first quarter of 2026). As a result, the method-of-use patents cannot explain a delay into 2026.

315. As to the three polymorph patents, Celgene had no colorable basis to prosecute to conclusion infringement litigation based on them. As previously alleged, these patents were applied for *after* the generic companies had developed their ANDA products and served paragraph IV notices; it could not be the case that both the generics' products infringed the polymorph patents and that the polymorph patents were not obvious over the prior art, *i.e.*, the ANDAs. Celgene had no ability to protect its pomalidomide franchise against the filed ANDA applicants with these patents.

316. As to the three formulation patents, one of those patents (the '427 formulation patent) was withdrawn from litigation by Celgene (at least by December 2020). Because Celgene could not prosecute patent infringement litigation based on it, that patent cannot explain the 2026 agreed entry date.

317. The remaining two formulation patents—the '467 and the '5939—were both set to expire on May 19, 2030. That date, extending as it does into the future, is quite telling. Celgene did not even bother to apply for these patents until well after all or nearly all the Pomalyst ANDAs were filed (in the case of the '5939, approximately *three years* later.) The notion that these patents are somehow essential to Pomalyst (and thus capable of blocking generic entry) is not credible. In any event, both patents were obtained based on the fraudulent Tutino declarations and are therefore unenforceable, as well as invalid as obvious over the prior art. The claims of the formulation patents are also quite narrow and would be easy for a generic manufacturer to design around.

318. *Second*, Celgene protected Natco/Breckenridge's risk of forfeiting their 180-day statutory exclusivity. As alleged above, Natco/Breckenridge had failed to obtain tentative or final approval within 30 months—which put them at risk of forfeiting their 180-day exclusivity. Celgene knew of this potential forfeiture. As such, Celgene and Natco/Breckenridge agreed to remove the risk of competition that would ensue if the FDA determined that one or more first filers forfeited by

conferring contractual exclusivity on Natco/Breckenridge. Although a year later, on December 6, 2021, the FDA determined—in its letter granting tentative approval to Dr. Reddy's—that the first filers had not forfeited their 180-day exclusivity; that does not change the fact that, a year earlier, Celgene and Natco/Breckenridge had already protected that forfeiture risk through their anticompetitive settlement agreement.

319. *Third*, Natco's earlier anticompetitive dealings with Celgene in settling lenalidomide litigation indicate that the pomalidomide Celgene-Natco settlement agreement was similarly anticompetitive and contains a reverse payment.

320. Several years earlier in 2015, Celgene and Natco had settled patent litigation over Natco's (and Teva's) proposed generic for Revlimid (lenalidomide) through an anticompetitive reverse payment agreement. That agreement explicitly contained market allocation arrangements under which Celgene and Natco agreed to have Natco delay all generic entry until 2022. In that arrangement, the parties agreed upon volume caps for total lenalidomide capsules dispensed, and the caps were to end in January 2026. Natco has disclosed that the volume-limited license is royalty free, meaning Natco has no obligation to pay Celgene a portion of its profits, as is the norm. The agreement also contained a most-favored entry clause to coordinate entry dates amongst would-be generics. Both by design and effect, Celgene and Natco worked on an arrangement for lenalidomide to delay generic entry until 2022, and even then, maintain supra-competitive pricing of lenalidomide until 2026.

321. Individually and collectively, these payment terms are anticompetitive. As Teva (Natco's Revlimid marketing partner) described it: with their lenalidomide settlements, Celgene set up a "profit share." The royalty-free generic license prior to true generic competition constitutes a large reverse payment from Celgene to the generic that equates to hundreds of millions of dollars in the first year of generic sales alone. And the most-favored entry clause deters other generics from

continuing to challenge Celgene's patents and provides assurance to Natco that it will receive the most favorable entry date and retain its lucrative exclusivity period.

322. Celgene would continue this pattern with other generics, engaging in a series of payoffs to would-be lenalidomide competitors. In the lenalidomide settlements, Celgene's payoffs took the form of market allocation agreements in which Celgene sequentially granted small, volume-limited licenses to each generic company to sell lenalidomide starting in 2022 and going to early 2026 (at which time there would be unconstrained competition). The volume-limited license agreements, which also contain no royalties to Celgene, significantly reduce the extent of the price reduction and effectively allocate the market amongst competitors. In design and effect, the lenalidomide volume-limited licenses function to have Celgene pay off would-be generic competitors by having them share, over a four-year period (early 2022 to early 2026), supra-competitive profits for lenalidomide. And Celgene entered these lenalidomide arrangements both several months before and several months after cutting the November 2020 pomalidomide Celgene-Natco agreement.

323. Celgene and Natco worked anticompetitive arrangements in the past by settling patent litigation and did so with respect to a product used in a complementary way to treat the same conditions. The date for *bona fide* agreed entry in the lenalidomide settlement is the first quarter of 2026—the same quarter in which the Celgene-Natco agreement delays pomalidomide entry. Celgene had already been a repeat offender in reaching anticompetitive, market allocation agreements by the time it reached the Celgene-Natco agreement. In short, the Celgene-Natco agreement for pomalidomide is designed to protect the illegal market allocation profit-sharing agreements that Celgene had created for lenalidomide.

324. *Fourth*, the Celgene-Natco agreement ensured that the companies that were engaging in the lenalidomide market allocation profit-sharing agreement would protect that illegal asset.

325. *Fifth*, the secrecy of the pomalidomide settlement also indicates the anticompetitive nature of the Celgene-Natco agreement, including by indicating the presence of a reverse payment.

326. Under the settlement, the parties apparently agreed to keep secret *all* the specific terms of the settlement, even the agreed entry date, for some period. For example, during earnings call on November 13, 2020, analysts repeatedly pressed Natco's CEO Rajeev Nannapaneni for the most basic information about the terms of the settlement. The CEO declined to provide any information, stating at one point, "I already answered the question, but I will just repeat it one more time. . . . we will not disclose the [generic launch] date because the settlement agreement was very particular that we do not talk about the date."

327. The parties kept the entry date secret for about a year and a half. Eventually in February 2022 —and only after settling with all the other would-be pomalidomide generic entrants—BMS disclosed the entry date to the public. There would be no generic entry into the pomalidomide market until the first quarter of 2026: "As it relates to U.S. IP for Pomalyst, we are pleased that there is now no outstanding litigation. At this point, we don't expect generic entry in the U.S. market prior to the first quarter of 2026."

328. The parties publicly disclosed only that (i) the parties settled all pomalidomide litigation between them, and (ii) the agreed entry date would be in the first quarter of 2026. The parties also disclosed that there are other terms of the agreement, but refused to disclose any further information about the additional terms to the public.

329. To settle Hatch-Waxman patent litigation, it is sufficient for the parties to settle based on an agreed entry date; nothing more is required. In fact, the FTC published a study finding that from 2004 through 2009, seventy percent of final settlements agreements (152 out of 218) "did not involve compensation from the brand to the generic combined with a delay in generic entry." As the FTC explained, "[t]his large number of settlements not involving compensation from the brand

to the generic undermines brand and generic firms' arguments that compensation is the only way to settle patent litigation. In fact, there are a variety of ways to settle litigation that do not involve these payments."[106] In settling based on an agreed entry date and only an entry date, the settlement is likely assured to be based on the relative merits of the parties' positions in the underlying patent litigation. But when the parties add additional consideration (such as payments) going to the settling generic in the agreement, it is likely that non-patent-merits considerations are influencing the agreed entry date.

330. Here, the Celgene-Natco agreement contains provisions other than the agreed entry date, and the parties conceal those other terms. Taken in the context of all other facts, this further shows that the Celgene-Natco agreement includes a large, unjustified payment to the Natco parties. While the settling parties to the Celgene-Natco agreement have had some success keeping the specific *form* of the reverse payment secret, they have not been able to conceal the *existence and size* of the reverse payment.

331. *Finally*, the likelihood of anticompetitive provisions in the Celgene-Natco agreement is shown by the fact that similar agreements between Celgene and Natco have failed review by competition authorities outside the U.S. These authorities apply competition principles similar to those in the U.S.

332. For example, on December 3, 2021, Celgene and Natco submitted settlement/licensing agreements for Pomalyst and Revlimid to the Australian Competition and Consumer Commission (ACCC) for approval. On March 23, 2022, the ACCC issued a Draft Determination recommending rejection of the application, stating the "ACCC considers the settlement and license agreement is likely to result in public detriment by reducing competitive

[106] FTC, *Pay-for-Delay: How Drug Company Pay-Offs Cost Consumers Billions*, 4, (2010) available at https://www.ftc.gov/reports/pay-delay-how-drug-company-pay-offs-cost-consumers-billions-federal-trade-commission-staff-study (last accessed August 21, 2024).

tension in relation to generic entry in the supply of lenalidomide and pomalidomide. The ACCC considers the settlement and license agreement provides Celgene with greater control and certainty over the timing of generic entry by Juno/Natco, seeks to confer on Juno/Natco a 'first mover advantage', may deter other generic entry, [REDACTED]." On July 29, 2022 (the eve of the deadline for the ACCC's final determination), Celgene and Natco withdrew their application. One report about the incident wrote "the ACCC's draft determination marks one of the first opportunities the regulator has had to consider a reverse payment settlement in the Australian context — and is likely to have a chilling effect on similar applications for the foreseeable future."

333. Under the Celgene-Natco agreement, the value of the payment from BMS/Celgene to Natco/Breckenridge is substantial, certainly magnitudes larger than Celgene's avoided litigation expenses, and likely well into the nine figures (*i.e.*, of about $150 to $300 million).

334. The size of Celgene's *de facto* payment to Natco/Breckenridge may be estimated as follows. Under normal market conditions, after several months of *bona fide* generic entry, the generic penetration rate is typically 90%. If the only ANDA generic to enter the market was Natco/Breckenridge, a single first filer with 180 days of exclusivity would expect to take roughly half of these generic sales (with the other half of generic sales going to the brand company's authorized generic product, assuming it would also enter the market). Facing competition from the brand product and the authorized generic, the generic product is typically priced at approximately 60% of the brand price. Applying those figures to the pomalidomide market, during the first six months, a generic company with exclusivity would expect sales of about $300 million ($2.25 billion in 2021 U.S. sales x 0.5 years x 90% of the market is generic x 50% of generic market x 60% price of the brand).

335. Even if both Natco/Breckenridge and Aurobindo (the two companies with final ANDA approvals as of November 2020) were to enter the market (thereby sharing the 180-day

exclusivity period), the revenues from the generic products would be divided by a third each (the two ANDA generic products and the authorized generic product). In addition, the presence of an additional generic would likely have caused some degree of additional price erosion. However, each of the ANDA filers would still expect to earn about $167 million ($2.25 billion in 2021 U.S. sales x 0.5 years x 90% of the market is generic x 33% of generic market x 50% price of the brand).

336. As a result, a reasonable company in the position of Natco/Breckenridge in November 2020, having first-to-file status and being one of only two finally approved ANDA applicants, would expect to achieve about $167 to $300 million in revenues over six months were it to launch generic pomalidomide and exploit a period of oligopolistic pricing.

337. On the other hand, because of the reverse payment in the Celgene-Natco agreement settlement with Celgene, Natco/Breckenridge agrees to wait six years and not launch its approved ANDA pomalidomide product until early 2026. At that time, the market expectation is that all or most of the *other* first-to-file generics would by then have obtained their final ANDA approvals. And as this was a classic, post-NCE pile-on (where multiple generics file ANDAs on the first allowed date, and at least seven generics filed on the same date with first-to-file status), the expectation would be that, after waiting six years to enter in early 2026, the entry by Natco/Breckenridge would occur into an immediately, fully genericized market.

338. In a fully genericized market, generic penetration is about 90%, the price discount is often about the same (or larger), and most generics estimate similar shares of the market. Even assuming the pomalidomide market would grow at 5% a year, by waiting for six years to enter in the first quarter of 2026, a reasonable company in the position of Natco/Breckenridge would expect to achieve about $19.4 million over six months. (Projected $3.02 billion in 2026 U.S. sales x 0.5 years x 90% of the market is generic x 0.143 (*i.e.*, $1/7^{th}$ of the generic market) x 10% of the brand).

339. The enormous difference between the reasonably estimated returns under these circumstances ($167-$300 million over the first six months from imminent launch, versus about $19.4 million under the settlement and six years later) requires significant compensation to Natco/Breckenridge for the settlement.

340. In sum, the Celgene-Natco agreement contains an anticompetitive, reverse payment arrangement which functions to delay and/or impair generic entry of pomalidomide into the U.S. market.

2. March 2021: The Celgene-Teva reverse payment agreement.

341. In or about March 2021, Celgene and BMS, on the one hand, and the Teva defendants, on the other, settled the pending pomalidomide litigation between them (the "Celgene-Teva agreement") under terms that provide for a large, unjustified payment from Celgene/BMS to Teva. In return, Teva agreed to delay entry into the U.S. pomalidomide market until six years later, *i.e.*, the first quarter of 2026. The terms of the arrangement were in part reflected in documentation, but also by the combined *de facto* economics of the industry and incentives created by the agreement.

342. The Celgene-Teva agreement does not represent a *bona fide*, arms-length resolution of the merits of the pomalidomide litigation.

343. Several facts, when viewed together, reveal the existence of a large, unjustified payment from Celgene/BMS to Teva and the anticompetitive nature of the agreement. *First*, as described above, Celgene's patents (several of which expire before the agreed-to entry date or were withdrawn prior to settlement) are weak and cannot explain the extended delay in generic entry.

344. *Second*, Teva (through its affiliate Arrow, which partnered with Natco on Revlimid) and Celgene entered into an agreement to settle their Revlimid (lenalidomide) litigation in 2015. That settlement agreement, involving the same parties and a complementary drug, provided for a volume-limited, royalty free license and most favored entry clauses. The Revlimid settlement agreement

between Celgene and Teva functions as an unlawful market allocation agreement to restrict competition and keep prices at supra-competitive levels until sometime after the first quarter of 2026. The agreement also effectuates a substantial, unjustified payment to Teva by cutting Teva in on Celgene's and BMS's monopoly profits.

345. *Third*, the secrecy of the pomalidomide settlement also indicates the anticompetitive nature of the Celgene-Teva agreement, including the existence of a reverse payment. Although Teva and Celgene had settled their Pomalyst dispute by early March 2021, all information, including even the fact of settlement, was concealed for nearly a year. When the Pomalyst settlements were finally announced by BMS in February 2022, it was revealed that all generics, including Teva, have agreed to delay their entry date until the first quarter of 2026.

346. The Celgene-Teva agreement contains additional provisions beyond the agreed entry date, and the parties seek to conceal those other terms. Again, as explained above, to settle Hatch-Waxman patent litigation, nothing more is required beyond the parties settling based on an agreed entry date. When the parties add additional consideration (such as payments) going to the settling generic in the agreement, it is likely that non-patent-merits considerations are influencing the agreed entry date.

347. Taken in the context of all other facts, this further shows that the Celgene-Teva agreement provides of a large, unjustified payment to the Teva parties. Although the settling parties to the Celgene-Teva agreement have had some success keeping the specific form of the reverse payment secret, they have not been able to conceal the existence and size of a reverse payment. The value of the payment from BMS/Celgene to Teva is substantial, certainly magnitudes larger than Celgene's avoided litigation expenses, and likely well into the nine figures.

348. Teva adhered to the secret agreement, refraining from launching generic Pomalyst, despite receiving FDA final approval on May 4, 2022.

349. In sum, the Celgene-Teva agreement contains an anticompetitive, reverse payment arrangement which functions to delay and/or impair generic entry of pomalidomide into the U.S. market.

3. Spring 2021: The Celgene-Aurobindo reverse payment agreement.

350. On or about July 16, 2021, Aurobindo (which had also received final approval on October 30, 2020) and Celgene notified the court that they had resolved their dispute as to the Pomalyst patents. Aurobindo had earlier discontinued its ANDA.

351. Celgene and BMS, on the one hand, and the Aurobindo defendants, on the other, settled the pending pomalidomide litigation between them (the "Celgene-Aurobindo agreement") under terms that provide for a large, unjustified payment from Celgene/BMS to Aurobindo. In return, according to Celgene and BMS's public statements, Aurobindo agreed to delay entry into the U.S. pomalidomide market until six years later, *i.e.*, on a date strategically timed such that all other first-to-file generics would have the same agree entry date—the first quarter of 2026.

352. The terms of the arrangement were in part reflected in documentation, but also by the combined *de facto* economics of the industry and incentives created by the agreement.

353. The Celgene-Aurobindo agreement does not represent a *bona fide*, arms-length resolution of the merits of the pomalidomide litigation.

354. Several publicly disclosed facts, particularly when viewed together, show the existence of a large, unjustified payment from Celgene to Aurobindo and the anticompetitive nature of the agreement. *First*, again, as described above, Celgene's patents (several of which expire before the agreed-to entry date or were withdrawn prior to settlement) are weak and cannot explain the extended delay in generic entry.

355. *Second*, Celgene protected Aurobindo's risks of forfeiting its 180-day statutory exclusivity. As alleged above, Aurobindo had failed to obtain tentative or final approval within 30

months—which put it at risk of forfeiting its 180-day exclusivity. Celgene knew of this potential forfeiture. As such, Celgene and Aurobindo agreed to remove the risk of competition that would ensue if the FDA determined that one or more first filers forfeited, by conferring contractual exclusivity on Aurobindo. Although the FDA stated six months later that the first filers had not in fact forfeited their 180-day exclusivity (in its letter granting tentative approval to Dr. Reddy's), Celgene and Aurobindo had already protected that forfeiture risk through their anticompetitive settlement agreement.

356. *Third*, Aurobindo and Celgene also entered into an agreement to settle their earlier Revlimid (lenalidomide) litigation—notably, the parties ended their disputes regarding Revlimid and Pomalyst *on the same day,* filing consent decrees in both matters on July 16, 2021. The Revlimid settlement agreement, involving the same parties and a complementary drug, provided for a volume-limited, royalty free license and most favored entry clauses—capping the generic's lenalidomide sales until the first quarter of 2026 (when generic Pomalyst entry begins). Like with Celgene's Revlimid settlements with Natco and Teva, the Revlimid settlement agreement between Celgene and Aurobindo functions as an unlawful market allocation agreement to restrict competition and keep prices at supra-competitive levels until sometime after the first quarter of 2026. The agreement also effectuates a substantial, unjustified payment to Aurobindo by cutting Aurobindo in on Celgene's and BMS's monopoly profits. After all, the Revlimid market share profit-split is worth substantial sums to Aurobindo, likely in the nine figures.

357. As alleged above, Celgene had already been a repeat offender in reaching anticompetitive, market allocation agreements by the time it reached the Celgene-Aurobindo agreement. In short, the Celgene-Aurobindo agreement for pomalidomide is designed to protect the illegal market allocation profit-sharing agreements that Celgene had created for lenalidomide.

358. *Fourth*, the secrecy of the pomalidomide settlement also indicates the anticompetitive nature of the Celgene-Aurobindo agreement, including the existence of a reverse payment. In fact, Aurobindo and Celgene have concealed the terms of both their Revlimid and Pomalyst settlement agreements.

359. Although it was revealed that all generics, including Aurobindo, have agreed to delay their entry date until the first quarter of 2026, the Celgene-Aurobindo agreement contains provisions beyond the agreed entry date. Like with the Celgene-Natco and Celgene-Teva agreements, the parties in the Celgene-Aurobindo agreement seek to conceal those other terms. Again, as explained above, when parties add additional consideration such as payments for the settling generic, it is likely that non-patent-merits considerations are influencing the agreed entry date.

360. Taken in the context of all other facts, this further shows that the Celgene-Aurobindo agreement provides a large, unjustified payment to the Aurobindo parties. Although the settling parties to the Celgene-Aurobindo agreement have had some success keeping the specific form of the reverse payment secret, they have not been able to conceal the existence and size of a reverse payment. The value of the payment from BMS/Celgene to Aurobindo is substantial, certainly magnitudes larger than Celgene's avoided litigation expenses, and likely well into the nine figures.

361. Aurobindo adhered to the secret agreement, refraining from launching generic Pomalyst, despite receiving final FDA approval on October 30, 2020. Had Aurobindo launched its generic Pomalyst immediately, it would have earned between $167 to $300 million in the first six months alone. Instead, Aurobindo agreed to delay market entry for six years. This means that, absent some other terms to compensate Aurobindo, Aurobindo would earn only approximately $19.4 million over the first six months of entry if launching into a fully genericized market in 2026.

362. The enormous difference between the reasonably estimated returns under these circumstances ($167-$300 million over the first six months from imminent launch, versus about $19.4 million under the settlement and six years later) requires significant compensation to Aurobindo for the settlement.

363. In sum, the Celgene-Aurobindo agreement contains an anticompetitive, reverse payment arrangement which functions to delay and/or impair generic entry of pomalidomide into the U.S. market.

Q. February 2022: Celgene revealed that all generic pomalidomide entry is delayed until early 2026.

364. To this point in time, Celgene, BMS, and the settling generics had withheld all information about the Pomalyst settlements and concealed their terms.

365. It was not until a February 4, 2022 earnings call that BMS disclosed for the first time that there would be no generic entry for Pomalyst until the first quarter of 2026.

366. This meant that, in addition to Celgene's illegal reverse payment agreements with Natco/Breckenridge, Aurobindo, and Teva, Celgene also reached settlement agreements with Hetero, Apotex, Mylan (another generic that discontinued its ANDA after receiving final approval), Par, Dr. Reddy's, and Synthon/Alvogen (the "Additional Settling Generics"). Celgene and the Additional Settling Generics have concealed all information about their Pomalyst settlements, other than to disclose that no generic will enter the market prior to the first quarter of 2026.

367. Moreover, like Natco/Breckenridge, Aurobindo, and Teva, nearly all the Additional Settling Generics that had a Pomalyst ANDA also had a Revlimid ANDA. After Celgene sued them for infringement of Celgene's Pomalyst and Revlimid patents, a generic often settled the two matters concurrently:

ANDA filer(s)	Date Pomalyst consent judgment filed with the court	Date Revlimid settlement disclosed to the public

Alvogen	May 9, 2019	March 29, 2019
Apotex	April 19, 2021	March 9, 2021
Hetero	August 18, 2021	September 24, 2021
Mylan	N/A – November 2021 is estimated settlement date.	July 21, 2021
Dr. Reddy's	January 28, 2022	September 17, 2020

368. In July 2022, BMS confirmed – for the first time – that it had obtained "a longer than previously expected market exclusivity period for Pomalyst."

369. At a minimum, Celgene's settlement agreements with the Additional Settling Generics ensure that the illegal reverse payment agreements will function as intended, delaying generic Pomalyst entry and ensuring supra-competitive pricing for at least six years beyond what would have occurred absent the unlawful reverse payment agreements.

R. Because generic competition will not begin until early 2026, CenterWell will continue to suffer substantial overcharges on its purchases of Pomalyst.

370. Celgene's and BMS's scheme to extend and maintain a monopoly in the market for Pomalyst and its generic equivalents worked. Celgene and BMS have prevented generic competition for Pomalyst until 2026. As a result, CenterWell has been and will continue to be forced to purchase brand Pomalyst at supra-competitive prices through at least that time.

371. Shortly after announcing the settlements, BMS acknowledged that it was able to achieve a longer delay in generic entry than previously expected. In its quarterly report for the first quarter of 2022, BMS reported: "Amortization of acquired intangible assets decreased by $96 million in the first quarter of 2022, due to a longer than previously expected market exclusivity period for Pomalyst." In other words, BMS reported that during the quarter that it announced all Pomalyst patent litigation had been settled, BMS's expectations regarding its exclusivity period for Pomalyst had changed, *because it now expected its exclusivity period to last longer than previously expected*, further

indicating that the settlement agreements provided for a generic delay period that exceeds what one would have expected based on the patents alone.

372. Absent Celgene's and BMS's anticompetitive conduct, generic Pomalyst would have been available years ago, on a date to be determined during discovery and as early as October 30, 2020 (when Natco/Breckenridge received final approval).

373. Absent the Pomalyst agreements, under competitive conditions, a reasonable generic company in the positions of the generic companies would have: (i) launched generic Pomalyst after prevailing at trial, (ii) launched at risk at some point after obtaining final approval, or (iii) entered into an arm's length, payment-free agreement that provides for unrestricted sales and/or an earlier, risk-adjusted, agreed entry date. Absent Celgene's and BMS's anticompetitive conduct, reasonable generics, not seeking to protect unlawfully obtained supra-competitively priced sales, would have launched as early as October 30, 2020.

374. A 2010 study by the FTC found that on average, within a year of generic entry, generics had captured 90% of corresponding brand sales and (with multiple generics on the market) prices had dropped 85%, findings confirmed by later studies. Given that there were multiple generic filers, it is likely that additional generics would have entered subsequent to Natco/Breckenridge, driving down prices in accord with industry experience.[107] Thus, CenterWell will suffer substantial damages in overcharges on its Pomalyst purchases through at least early 2026.

[107] Conrad, R., and R. Lutter. (2019). *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Generic Drug Prices*. FDA, available at https://www.fda.gov/media/133509/download (last accessed August 21, 2024).

VI. MARKET POWER AND RELEVANT MARKET

375. The relevant product market is brand Pomalyst and its AB-rated generic equivalents. Since 2013, Celgene (and BMS since its acquisition of Celgene) has possessed monopoly power in the United States with respect to this market by virtue of its 100% market share.

376. In the pharmaceutical marketplace, there is a disconnect between product selection and payment. State laws prohibit pharmacists from dispensing many pharmaceutical products, including Pomalyst, to patients without a prescription. Patients must obtain prescriptions from their physicians. However, a patient's physician has no role in the purchase of the prescription medication. The patient's doctor chooses which product the patient will buy, while the patient (and in most cases his or her insurer) must pay for it.

377. Brand manufacturers, including Celgene and BMS, exploit this disconnect by employing large sales forces that visit doctors' offices and persuade them to prescribe the brand manufacturers' products. These sales representatives do not advise doctors on the cost of their branded products. Studies show that doctors are typically unaware of the relative costs of brand pharmaceuticals and, even when they are aware, are largely insensitive to price differences because they do not pay for the products. The result is a marketplace where price plays a comparatively unimportant role in product selection.

378. The relative unimportance of price in the pharmaceutical marketplace reduces what economists call the own-price elasticity of demand—the extent to which unit sales go down when price goes up. This reduced-price elasticity enables brand manufacturers to raise prices substantially above marginal cost without losing enough sales to make the price increase unprofitable. The ability to profitably raise prices substantially above marginal costs is what economists and antitrust courts refer to as market power. Economists refer to monopoly power when market power rises to a level as would be held by a dominant firm. The result of these pharmaceutical market imperfections and

marketing practices is that brand manufacturers gain and maintain monopoly power with respect to many brand prescription pharmaceuticals, including Pomalyst.

379. Celgene and BMS have monopoly power in the market for Pomalyst because they have the power to exclude competition and raise or maintain the price of Pomalyst to supra-competitive levels without losing enough sales to make these prices unprofitable.

380. Celgene and BMS need control only brand Pomalyst, and its AB-rated generic equivalents, and no other products, in order to maintain the price of Pomalyst profitably at supra-competitive levels. Only the market entry of competing, AB-rated generic versions of Pomalyst would render Celgene and BMS unable to profitably maintain its prices for Pomalyst without losing substantial sales.

381. For years, Celgene and BMS have sold Pomalyst at prices well in excess of marginal costs and in excess of the competitive price. Therefore, Celgene and BMS had high profit margins.

382. Celgene and BMS had, and exercised, the power to exclude generic competition to brand Pomalyst.

383. At all relevant times, Celgene and BMS were protected by high barriers to entry due to patent protection, the high cost of entry and expansion, expenditures in marketing and physician detailing, and state statutes that require prescriptions for the purchase of the products at issue and restrict substitution of those products at the pharmacy counter. The products in these markets require significant investments of time and money to design, develop, and distribute. In addition, the markets require government approvals to enter and/or the drugs at issue may be covered by patents or other forms of intellectual property. Celgene's and BMS's unlawful conduct further restricted entry. Thus, during the relevant time, existing and potential market entrants could not enter and/or expand output quickly in response to Celgene's higher prices or reduced output.

384. There is direct evidence of market power and anticompetitive effects available in this case sufficient to show Celgene's and BMS's ability to control the price of Pomalyst, and to exclude relevant competitors, without the need to define the relevant antitrust markets. The direct evidence consists of, *inter alia*, the following facts: (1) generic Pomalyst would have entered the market at a much earlier date, at a substantial discount to brand Pomalyst, but for Celgene's anticompetitive conduct; (2) Celgene's and BMS's gross margin on Pomalyst at all relevant times was very high; (3) Celgene and BMS never lowered the price of Pomalyst to the competitive level in response to the pricing of other brand or generic drugs; and (4) from 2013 through 2022, Celgene (and BMS after its acquisition) profitably raised the price of Pomalyst by more than 200%.

385. To the extent proof of monopoly power by defining a relevant product market is required, CenterWell alleges that the relevant antitrust market is the market for Pomalyst and its AB-rated generic equivalents.

386. The United States, the District of Columbia, and the U.S. territories constitute the relevant geographic market.

387. Celgene and BMS will have a 100% market share in the relevant market until the 2026 agreed-to entry date.

VII. EFFECT ON INTERSTATE COMMERCE

388. During the relevant time period, Celgene and BMS manufactured, sold, and shipped Pomalyst across state lines in an uninterrupted flow of interstate commerce.

389. During the relevant time period, CenterWell purchased, paid for, and/or provided reimbursement for some or all of the purchase price for Pomalyst and/or pomalidomide. As a result of Celgene's and BMS's illegal conduct, CenterWell was compelled to purchase brand Pomalyst at supra-competitive prices.

390. During the relevant time period, Celgene and BMS used various devices to effectuate the illegal acts alleged herein, including the United States mail, interstate and foreign travel, and interstate and foreign wire commerce. Defendants engaged in illegal activities, as charged in herein, within the flow of—and substantially affecting—interstate commerce, including in this district.

VIII. CLAIMS FOR RELIEF

COUNT ONE

VIOLATION OF 15 U.S.C. § 2
UNLAWFUL MONOPOLIZATION:
DAMAGES, DECLARATORY AND INJUNCTIVE RELIEF

391. CenterWell hereby repeats and incorporates by reference each preceding paragraph as though fully set forth herein.

392. At all relevant times, Celgene (and subsequently Celgene and its new parent BMS) possessed substantial market power (*i.e.*, monopoly power) in the relevant market. Celgene, and later Celgene and BMS, possessed the power to control prices in, prevent prices from falling in, and exclude competitors from, the relevant market.

393. Through the overarching anticompetitive scheme, as alleged above, Celgene and BMS defrauded the patent office to obtain invalid patents, engaged in sham litigation, and induced generics to delay their market entry by inducing settlements with unlawful reverse payments.

394. Celgene and BMS willfully maintained monopoly power in the relevant market using restrictive or exclusionary conduct, rather than by means of greater business acumen or a historic accident. Because of this unlawful maintenance of monopoly power, CenterWell paid artificially inflated prices for Pomalyst, and was thereby injured. Celgene's and BMS's anticompetitive conduct was done with the specific intent to maintain a monopoly in the market for brand and generic Pomalyst in the United States.

395. Defendants Celgene and BMS, together with Zeldis, and Insogna, knowingly and intentionally engaged in an anticompetitive scheme designed to block and delay entry of AB-rated generic versions of Pomalyst to maintain their monopoly power by obtaining the method of treatment and formulation patents by fraud through misleading the patent examiner and/or Patent Office and failing to exercise the duty of good faith, then asserting these patents in sham litigations.

396. By means of this scheme, Celgene and BMS intentionally and wrongfully maintained monopoly power with respect to brand and generic Pomalyst in violation of Section 2 of the Sherman Act. As a result of this unlawful maintenance of monopoly power, CenterWell paid artificially inflated prices for its pomalidomide requirements.

397. Defendants' anticompetitive conduct are not entitled to qualified *Noerr-Pennington* immunity because Defendants enforced patents obtained by fraud, which warrants no First Amendment protection, and because Defendants filed waves of patent lawsuits that were intended to delay generic entry and which could not realistically expect to prevail.

398. Defendants Celgene and BMS, together with co-conspirators Zeldis and Insogna, engaged in distinct frauds on the patent examiner, actionable under *Walker Process*. Defendants made willful false representations and/or deliberate omissions of fact that were material, did so with intent to deceive the examiner, on which the examiner did in fact rely, and but for which the patents would not have issued.

399. First, Celgene obtained the method of treatment patents by misrepresenting that the '517 patent does not teach pomalidomide and D'Amato's 2001 study did not teach methods of using pomalidomide to treat multiple myeloma. Both Zeldis and Insogna made specific misrepresentations and omitted key prior art to carry out this fraud, including with respect to the '262 patent (which claims using pomalidomide for the treatment of multiple myeloma). The '262 patent will expire June 17, 2025.

400. In the absence of the Defendants' misrepresentations and/or omissions during prosecution of the method of treatment patents, none of the method of treatment patents would have issued, Celgene and/or BMS would not have had a pretextual basis for suing the first-filer generics for infringing the method of treatment patents, there would have been no attendant 30-month stay, and there would have been no opportunity for Celgene and BMS to settle litigation concerning the method of treatment patents on terms that kept generics out of the market until Q1 2026.

401. Second, Celgene obtained the formulation patents by falsely claiming unexpected results (and omitting facts that would have revealed the falsity of its unexpected results claim). Insogna made specific misrepresentations and omissions to carry out this fraud, including in prosecuting the application for the '427 patent, the first application in the formulation patent family. The '427 patent expires June 21, 2031.

402. In the absence of the Defendants' misrepresentations and/or omissions during prosecution of the formulation patents, none of the formulation patents would have issued, Celgene and/or BMS would not have had a pretextual basis for suing the first-filer generics for infringing the formulation patents, there would have been no attendant 30-month stay, and there would have been no opportunity for Celgene and BMS to settle litigation concerning the formulation patents on terms that kept generics out of the market until the first quarter of 2026.

403. The polymorph patents did not present a real bar to generic entry. They were filed months after the first-filer generics submitted their ANDAs and so could not trigger a 30-month stay. They were also easily designed around and highly unlikely to be novel.

404. Celgene's and BMS's anticompetitive activities have directly, foreseeably, and proximately caused injury to CenterWell throughout the United States. CenterWell's injuries consist of: (i) being denied the opportunity to purchase or provide payment and/or reimbursement for

lower-priced Pomalyst from Celgene and BMS, (ii) paying higher prices for brand and/or generic Pomalyst than it would have paid in the absence of Celgene's and BMS's unfair, illegal, and deceptive conduct, and (iii) being denied the opportunity to purchase or provide payment and/or reimbursement for generic versions of Pomalyst at a price substantially lower than what it was forced to pay for Pomalyst. These injuries are of the type that the laws of the jurisdictions below were designed to prevent, and they flow from that which makes Celgene's and BMS's conduct unlawful.

405. Celgene and BMS furthered their scheme by entering into unlawful agreements for delay in generic entry. They did so to lengthen the period in which Celgene's brand Pomalyst could monopolize the market, enabling Celgene and BMS to make supra-competitive profits.

406. Had Celgene and BMS competed on the merits instead of unlawfully maintaining a monopoly in the market for Pomalyst, one or more generic equivalents would have been available as early as October 30, 2020. CenterWell would have substituted lower-priced generic Pomalyst for the higher-priced brand-name Pomalyst for some or all of their Pomalyst requirements and would have paid substantially lower prices for brand-name Pomalyst and generic Pomalyst.

407. The goal, purpose, and effect of Celgene's and BMS's overarching anticompetitive scheme was to block generic drugs from entering the market for Pomalyst, extend their dominance in that market, and maintain Pomalyst's prices at supra-competitive levels. The scheme has had the further effect of depriving the market of competition.

408. Celgene's and BMS's scheme substantially harmed competition in the relevant market and was an unreasonable restraint of trade.

409. There is and was no non-pretextual, procompetitive justification for Celgene's or BMS's actions that outweighs the scheme's harmful effects. Even if there were some conceivable

justifications that Celgene or BMS could assert, the scheme is and was broader than necessary to achieve such a purpose.

410. But for Celgene's and BMS's illegal conduct, competitors would have begun marketing generic versions of Pomalyst beginning as early as October 30, 2020. CenterWell's allegations comprise a violation of Section 2 of the Sherman Act.

411. CenterWell has been injured in its business or property by reason of Defendants' antitrust violations. Its injury consists of having paid and continuing to pay higher prices for Pomalyst directly from Celgene and BMS, than it would have paid in the absence of Celgene's and BMS's violations. Such overcharges are the type of injury the antitrust laws were designed to prevent and flows from that which makes Celgene's and BMS's acts unlawful.

412. Even after generic competition begins, CenterWell and its subsidiaries will continue to pay supra-competitive prices for generic versions of Pomalyst until the market achieves equilibrium.

413. CenterWell seeks treble damages under Section 4 of the Clayton Act, 15 U.S.C. § 15, for its subsidiaries' direct purchases from Celgene and BMS of Pomalyst, and for CenterWell's subsidiaries' overpayments for generic Pomalyst, if and when it belatedly becomes available.

414. As a direct result of Defendants' violation of 15 U.S.C. § 2, CenterWell has been injured. Additionally, pursuant to Fed. R. Civ. P. 57 and 28 U.S.C. § 2201(a), CenterWell seeks a declaratory judgment that Celgene's and BMS's conduct in seeking to prevent competition as described in the preceding paragraphs violates Section 2 of the Sherman Act.

415. Pursuant to Section 16 of the Clayton Act, 15 U.S.C. § 26, and other applicable law, CenterWell further seeks equitable and injunctive relief to correct for the anticompetitive market effects caused by Celgene's and BMS's unlawful conduct and to assure that similar anticompetitive conduct does not occur in the future.

DEMAND FOR JUDGMENT

WHEREFORE, Plaintiff respectfully demands that this Court:

A. Enter joint and several judgments against the Defendants and in favor of CenterWell;

B. Award CenterWell treble damages (*i.e.*, three times overcharges) in an amount to be determined at trial;

C. Grant permanent injunctive relief pursuant to § 16 of the Clayton Act to remedy the ongoing anticompetitive effects of Celgene's and BMS's unlawful conduct;

D. Award CenterWell its costs of suit, including reasonable attorneys' fees as provided by law; and

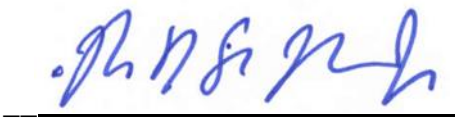
E. Award such further and additional relief as the case may require and the Court may deem just and proper under the circumstances.

JURY DEMAND

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, CenterWell demands a trial by jury on all issues so triable.

Dated: September 13, 2024

Respectfully submitted,



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